

Original Articles

ENCYSTED PLEURAL EFFUSIONS

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TEXTBOOKS of medicine make only casual mention of the occasional occurrence of encapsulated pleural effusions. They emphasize that it is the purulent pneumococcal effusion which most commonly becomes encysted. It is undoubtedly true that serous effusions are usually general effusions and not encysted. Nevertheless, having seen more than a few cases of encysted serous effusion occurring in various parts of the chest cavity, the writer is convinced that it is not as uncommon a condition as is generally believed.

Simple inflammation of the pleura (dry pleurisy) may be localized. Similarly, a localized effusion may occur, limited by surrounding adhesions. In pulmonary tuberculosis, particularly in those cases in which lung involvement has followed an attack of primary pleurisy, one frequently encounters adhesions during the attempted induction of artificial pneumothorax. These adhesions, evidently due to old localized pleurisy, are often found in places where the underlying lung is relatively free from disease, showing that in these cases the localized pleurisy is not due to contiguous spread from the lung, but has existed previously.

Inflammation can affect any portion of the pleura and, similarly, encysted effusions may be met with in any part of the chest cavity. In most cases the diagnosis can be made only by radiography. The object of this paper is not only to emphasize the importance of radiography in diagnosis, but also to record a few physical signs which are diagnostic of encysted effusions in certain situations.

Anatomical considerations.—The parietal and visceral pleura lines a potential free cavity. This free space extends outside the parietal surface of the lung, below the diaphragmatic surface, above the apex, and medial to the mediastinal surface excepting the portion occupied by the root of the lung and the ligamentum latum. A potential free space also exists between the lobes of the lung. While anatomy books emphasize the surface markings of the interlobar fissures, the clinician and the radiologist are more concerned with the extent and the lie of the interlobar spaces.

The main interlobar fissure divides the lung into an antero-superior half and a postero-inferior half, held together by the root of the lung. The fissure rises steeply on the mediastinal surface above the hilum, and falls more

obliquely on the outer surface. On reaching the lower anterior margin of the lung, the fissure turns backwards along the diaphragmatic surface to gain the mediastinal surface, where it runs nearly vertically towards the hilum. Consequently, the upper part of the interlobar surface of the lower lobe looks forwards and outwards, while the lower part of this surface looks forwards and inwards. Hence its projection on the surface of the lung is 'propeller shaped.' It is very important to appreciate this in order to interpret correctly the x-ray shadow cast by an interlobar effusion.

In the right lung, there is an additional interlobar fissure, separating the upper from the middle lobe. The middle interlobar space is triangular with its apex directed forwards. The base of the triangle is formed by the junction of the middle fissure and the oblique fissure.

Pleural effusions may be classified anatomically as follows:—

1. Parietal.
2. Diaphragmatic.
3. Mediastinal.
4. Mediastino-interlobar.
5. Interlobar.
6. Extra-pleural.

Parietal effusion.—The commonest sites for encapsulation are the lateral wall and the posterior wall near the base. Encapsulation rarely occurs at the apex or on the anterior wall. In the costo-phrenic angle, a small effusion is common, and is frequently missed.

The classical signs of effusion—diminished resonance on percussion, diminished vocal resonance and fremitus, and weak breath sounds—are naturally confined to the part affected. In a lateral effusion, none of these signs will be found either in front or behind. Displacement of the mediastinum to the opposite side is rarely seen in encysted parietal effusions, but, in long-standing cases, the mediastinum is often displaced to the same side, probably owing to shrinkage of the lung.

In the radiogram an encapsulated parietal effusion shows a well-defined border with a convexity towards the lung. Sometimes these effusions take different shapes, depending on the exact site. Differential diagnosis from new growth of the lung has to be made by exploration and aspiration of the fluid. A small effusion in the costo-phrenic angle shows, in the radiogram, a triangular opacity obliterating the angle.

Case report 1.—A male, aged 24 years, had an attack of acute tonsillitis, and later had an intermittent temperature and complained of pain in the left side of the chest. For the first fifteen days, there were hardly any physical signs except slight diminution of breath sounds. No pleuritic rub was heard. Later, he developed signs of effusion on the left side, confined to the lateral wall. X-ray confirmed the diagnosis of encysted parietal effusion (figure 1, plate I). Exploration revealed serous fluid. A radiogram taken two years later showed the same shadow at the site of the effusion, but it was smaller and less dense. No fluid could be withdrawn. The patient was otherwise in good health.

Diaphragmatic effusion.—Shanks, Kerley and Twining (1938) are of opinion that a diaphragmatic effusion is invariably secondary to a sub-phrenic abscess. Barjon (1918) on the other hand reported cases of encysted diaphragmatic pleurisy. Acute fibrinous diaphragmatic pleurisy is not uncommon. Diaphragmatic effusions, however, are often missed, and the diagnosis is hardly ever made owing to the paucity of physical and radiological signs. The signs which should make one consider the possibility of diaphragmatic pleurisy are these: acute pain along the costal margin aggravated by deep breathing, and pain referred to the shoulder; these are associated with a raised temperature and pulse rate. A small effusion will not produce any physical signs at all. If, however, the effusion is fairly large and on the right side, the upper limit of hepatic dullness will appear to be raised. Whether this increased area of impaired resonance is due to an upward enlargement of the liver or to diaphragmatic effusion can be decided only by x-ray examination; usually there will be a band of opacity above and continuous with that of the diaphragm. The upper convex margin of the opacity will be parallel to the diaphragm. Often an effusion is localized to the centre of the diaphragm, and, in the x-ray picture, has the appearance of a hump on the diaphragm. The density of the fluid opacity will, however, be less than that of the liver. As the effusion becomes absorbed, changes in the shape of the shadow can be observed by serial photographs. After absorption of the effusion 'tenting' or 'peaking' of the diaphragm is common. The 'peak' is often continuous with the sclerosed lower portion of the main interlobar fissure.

Case report 2.—A patient, aged 33 years, complained of acute pain over the costal margin, difficulty in breathing, fever and dry cough. As there was rigidity and tenderness in the right hypochondrium coupled with referred pain over the shoulder, acute peri-hepatitis was thought of. Two days later the rigidity had disappeared, but pain over the right costal margin was still present. The liver was not palpable, but the upper level of hepatic dullness appeared to be raised. Radiography showed what looked like a large hump over the diaphragm (figures 2 and 3, plate I). This new shadow was however less opaque than that of the diaphragm. A provisional diagnosis of encysted diaphragmatic pleurisy was made. X-ray one month later showed that the hump had disappeared, leaving only a residual triangular opacity. The apex of the triangle was seen, in the lateral view, to be continuous with the sclerosed main interlobar fissure (figure 4, plate I).

Mediastinal effusion.—The root of the lung and the ligamentum latum divide the mediastinal pleural space vertically into anterior and posterior compartments. An effusion may be confined to either compartment, or may involve both simultaneously. When the effusion is in the right anterior compartment, the precordial area of dullness will be increased to the right, and the cardiac apex displaced to the left. Such signs, in the absence of other signs and

symptoms of cardiac disease, should make one think of a mediastinal effusion.

In an ordinary free parietal effusion, the whole mediastinum is displaced, as is evidenced by the displaced apex beat and trachea. A useful and interesting sign noted by the writer in cases of mediastinal effusion is that although the cardiac apex is displaced there is no displacement of the trachea. This sign is characteristic of mediastinal effusion.

Case report 3.—Male, aged 35 years, admitted to hospital with a dull aching pain in the left side of the chest, and irregular fever. On admission there were hardly any physical signs, but, after a week, slight impairment of resonance was noted on percussion of the left base. The apex beat was internal to the left mid-clavicular line, but the left margin of cardiac dullness was about one inch to the left of the normal. Resonance was normal in the back and side. There was slight impairment of resonance on percussion of the left costo-phrenic angle. The right border of the heart was shifted to the right. There was no displacement of the trachea. A radiogram showed a definite bulge on the left side of the cardiac opacity. The shadow cast by this bulge was so much less opaque than the cardiac shadow that the denser outline of the heart could be traced through the opacity. There was also a slight pleural 'haze' at the left base near the costo-phrenic angle (figures 5, 6 and 7, plates I and II). Radiography three weeks later showed no sign of the opacity.

Mediastino-interlobar effusion.—This type of pleurisy is more common in children. Fleischner (1926) first reported the condition. The effusion occurs in the lower end of the oblique fissure in its mediastinal half. Sometimes a mediastinal effusion co-exists. If mediastino-interlobar effusion occurs alone, then the diagnosis can be made only by radiography. In the ordinary antero-posterior view, an ill-defined triangular opacity is seen extending from the mediastinum with the apex of the triangle directed outwards and posteriorly. If the patient is asked to adopt the 'hollow back' position (bending backwards) while the picture is taken, the main fissure then becomes horizontal and the triangular opacity is very well defined. In the lateral view, the apex of the triangular opacity is found at the hilum level posteriorly while the base is in contact with the chest wall anteriorly.

Case report 4.—A patient, aged 19 years, complained of pain in the right side of the chest and continuous fever. For the first week there were no definite physical signs in the chest. Later examination revealed dullness and diminished breath sounds in the right cardio-hepatic angle. Resonance was normal behind and in the axilla. The heart was displaced to the left, but there was no deviation of the trachea. Radiography in the antero-posterior position showed a dense opacity extending from the right side of the heart to the periphery. Though there was a general 'haze', it was less dense in the costo-phrenic angle (figure 8, plate II). In the lateral view the spino-diaphragmatic angle was clear which would never be the case in a parietal effusion (figure 9, plate II). In the lordosis or 'hollow back' position, the radiograph showed a triangular opacity with the apex directed outwards and the base merging with the right border of the heart. It was evidently a case of effusion in the mediastinal portion of the interlobe combined with an anterior mediastinal effusion.

Interlobar effusion.—One or other of the fissures may be the site of effusion which may affect the whole or only a part of the interlobar space. When the effusion is sealed off from the general pleural cavity by the margins of the lobes, the diagnosis cannot be made without the help of the *x*-ray. A moderate effusion in the middle interlobar space gives a horizontal spindle-shaped shadow usually in the outer part of the middle lung field, because the fissure does not as a rule extend to the mediastinal surface. In the main fissure, the effusion lies obliquely; hence if it involves the whole extent of the fissure, a diffuse opacity is seen throughout the right side, but is limited below by a well-defined line representing the edge of the main fissure.

The most usual appearance of main interlobar effusion is a hatchet-shaped opacity in the middle of the lung. This opacity is separated from the heart shadow by a triangular area of the lung. The costo-phrenic angle is clear.

The lateral view is even more characteristic, because in this position the effusion is edged on to the rays and throws a clearer and better-defined shadow. Typical spindle-shaped shadows are seen lying in the line of the fissures. In the main fissure, if the effusion extends throughout its length, the shadow may be in the form of a double spindle. Effusion in the lower half alone may show a triangular outline with the apex at the level of the hilum and the axis directed obliquely forwards and downwards.

After absorption of the effusion, linear shadows may be seen in the line of the fissures owing to sclerosis of the interlobar pleura.

Case report 5.—(a) A male, aged 24 years, complained of vague pains in the right side of the chest, and had irregular fever. No definite physical signs were found. The *x*-ray picture, however, showed a typical elliptical shadow extending from the right cardio-phrenic angle, with the apex towards the periphery. The lateral view revealed that the shadow was in relation to the lower part of the main interlobar fissure. The condition cleared up in two months, and a subsequent *x*-ray showed only a sclerosed line in place of the original shadow.

(b) A patient, aged 21 years, had pain in the left side of the chest near the costal margin, and fever for fifteen days. Clinical examination showed impaired resonance in the left costo-phrenic angle in front, and the middle third of the left axillary region. A diagnosis of early pleural effusion was made. *X*-ray examination however showed an opacity above the left dome of the diaphragm and filling the costo-phrenic angle. The upper border of the opacity was a straight line running upwards and outwards. There was also an elliptical opacity in the parietal region (figure 10, plate II). The lateral view showed a long triangular band extending from the anterior costo-phrenic angle upwards and backwards towards the vertebral column (figure 11, plate II). This was evidently a case of effusion in the diaphragmatic portion of the main interlobar fissure with a small diaphragmatic effusion as well. There was also an encysted parietal effusion.

Extra-pleural effusion.—This type of effusion is rare and is never mentioned in the textbooks. It occurs invariably either as a post-trau-

matic condition or as a complication of extra-pleural artificial pneumothorax. The fluid is either hæmorrhagic or purulent. The writer has seen three instances of this condition following gunshot wounds in the region below the tenth rib in the posterior axillary line. In all three cases, the effusion seemed to have been a late sequela without manifest symptoms. In fact, the effusions were only discovered during routine chest *x*-ray examinations prior to discharge from hospital. Since this is a rare condition, the writer feels justified in discussing its pathogenesis in some detail.

Cunningham (1931) states that the diaphragmatic pleural reflection does not dip into the narrow potential space between the thoracic wall and the diaphragm. In other words a strip of the inner surface of the chest wall above the attachment of the diaphragm is left uncovered by the pleura. On dissecting this region in the post-mortem room cadavers, the writer found that the distance between the pleural reflection and the costal attachment of the diaphragm was greatest (about $\frac{3}{4}$ inch) in the posterior axillary line. A penetrating wound in this region may not, therefore, involve the pleura. If hæmorrhage occurs, it may excavate the extra-pleural space, since the parietal pleura can very easily be stripped. As the hæmorrhage will be encysted, it is not likely to cause any mediastinal displacement or respiratory embarrassment. Hence, such a hæmorrhagic effusion is apt to be 'silent'. A purulent effusion in the extra-pleural space may occur as a late sequela of a low-grade infection of a wound in this region.

Two of the patients seen by the writer had an encysted extra-pleural empyema. Both were symptomless. The diagnosis was confirmed by operation. In both cases the empyema followed a gunshot wound in the abdomino-thoracic junction in the posterior axillary line. Radiologically both showed a well-marked circumscribed opacity in the postero-lateral region near the base, with a well-defined convex margin internally. During operation it was found that the parietal pleura was absent over the part of the chest wall corresponding to the empyema cavity. The third case, also following a gunshot wound in the same region, presented a very interesting picture on *x*-ray examination. There was a general 'haze' involving the lower two-thirds of the right side of the chest. The upper limit of the haze was well defined by a curved line with its convexity upwards. In the centre of the haze there was a clear space without any opacity except normal lung markings. The clear space was about three inches by two inches in size, and oval in shape. The lateral view showed a thin strip of opacity in the postero-lateral region. Evidently a thin film of effusion had stripped the pleura in the postero-lateral region, leaving an island of adherent pleura in the middle of the excavation.

Summary

(1) The anatomy of the pleural cavity is described in brief.

(2) Different types of encysted effusion, depending on the position, are considered in detail.

(3) Case reports illustrating the types are given.

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THE PATHOGENESIS OF PULMONARY ATELECTASIS

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BEFORE discussing the pathogenesis of atelectasis, three illustrative cases are described, each having a different aetiology. It is proposed to show later that even though the precipitating factor in each of the cases is different, the ultimate mechanism by which atelectasis is produced is essentially the same.

Case 1.—A male, aged 26 years, was admitted to hospital for fever and cough of 10 days' duration. The fever was continuous and ranged between 100°F. and 102°F. Respiration was not hurried. A diagnosis of bronchiolitis was made. A week later the condition of the patient became worse. The range of temperature was higher. His breathing also was a bit more hurried. On examination, a triangular area of dullness was found in the left base behind, with bronchial breath sounds and a few moist sounds. The x-ray picture (figure 1, plate III) showed a triangular opacity overlapping the left border of the heart. In the lateral view the opacity was found to be situated posteriorly. A diagnosis of left lower lobe atelectasis was made. As the total leucocyte count was 14,000, he was put on sulphapyridine. The temperature came down only by lysis; his signs and symptoms disappeared only eight weeks after admission. An x-ray picture taken at the time showed that the opacity had disappeared (figure 2, plate III).

Case 2.—A male, aged 33 years, gave a history of a fall during which the left side of his chest struck against a projecting stone. Pain was so severe that he could not breathe for some time. There was no external injury. He spat out a little blood-tinged mucus after the injury. The pain lasted for a week. Subsequently he developed cough with expectoration. He had no temperature. But for a few moist sounds in the left base, no other physical signs could be elicited. X-ray examination (figure 3, plate III), however, showed a narrow well-defined triangular opacity, overlapping the cardiac shadow in the left side. The diagnosis of left lower lobe atelectasis was confirmed by a lateral x-ray picture.

Case 3.—A male, aged 24 years, said his trouble started by a fish bone slipping into the air passage while swallowing. He experienced difficulty in breathing, and an aching pain in the right side of the chest. Fever and cough started the next day. A few days

later he began to spit purulent sputum. Examination revealed impaired resonance and bronchial breath sounds over the right base. An x-ray picture (figure 4, plate III) showed a triangular opacity in the right cardiophrenic angle continuous with and obliterating the right border of the heart. A lateral view confirmed the diagnosis of right lower lobe atelectasis. Conservative treatment and postural drainage cleared up the condition in six weeks. An x-ray picture (figure 5, plate III) at the end of six weeks showed no opacity.

Intrapulmonary inflammation in the first case, external thoracic injury in the second case and frank bronchial obstruction by a foreign body in the third case brought about the same condition, namely, lower lobe atelectasis. Inflammatory exudate in the first case in all probability produced multiple bronchiolar obstruction while hæmorrhagic mucous secretion was the obstructing agent in the second case. The object of this paper is to show that bronchial or bronchiolar obstruction is the main contributing factor in the mechanism of collapse, and that it brings about the condition in two entirely different ways.

Current theories.—The pathogenesis of pulmonary atelectasis has been a subject of discussion for over a century. Even the earliest observers like Reynaud in 1835 and Hasse (1846) recognized the importance of bronchial obstruction in the aetiology of atelectasis. Gairdner (1851) regarded the blockage of bronchial tubes by retained secretion as the cause of collapse. Pasteur (1908), having seen massive collapse of the lung occurring during diphtheritic paralysis, postulated the theory of diaphragmatic paralysis to explain the occurrence of post-operative atelectasis. The experimental work of Briscoe (1920) appeared to confirm this theory. He pointed out that in the

EXPLANATION OF PLATES I AND II

- Fig. 1. *Case 1.*—Parietal effusion. Note well-defined opacity in the left parietal region with a sharp convex margin medially.
- Fig. 2. *Case 2.*—(a) Diaphragmatic effusion. Note the 'hump' over the right diaphragm.
- Fig. 3. *Case 2.*—(b) Diaphragmatic effusion after absorption. Note the 'peaking'.
- Fig. 4. *Case 2.*—(c) Lateral view of (b). Note the peak being continuous with sclerosed interlobar fissure.
- Fig. 5. *Case 3.*—Mediastino-interlobar effusion. (a) A.P. view.
- Fig. 6. *Case 3.*—(b) Lateral view showing clear spino-diaphragmatic angle.
- Fig. 7. *Case 3.*—(c) The same in the 'hollow back' position showing a more-or-less triangular opacity the base of which is continuous with a mediastinal opacity. Lines intensified by retouching.
- Fig. 8. *Case 4.*—Interlobar effusion. (a) A.P. view. Note the elliptical opacity.
- Fig. 9. *Case 4.*—(b) Lateral view. The elliptical opacity involves the lower part of the main fissure.
- Fig. 10. *Case 5.*—Interlobar effusion. (a) A.P. view showing an opacity in the left base and in the parietal region.
- Fig. 11. *Case 5.*—(b) Lateral view. Note the triangular band of opacity involving the lower part of the main fissure.

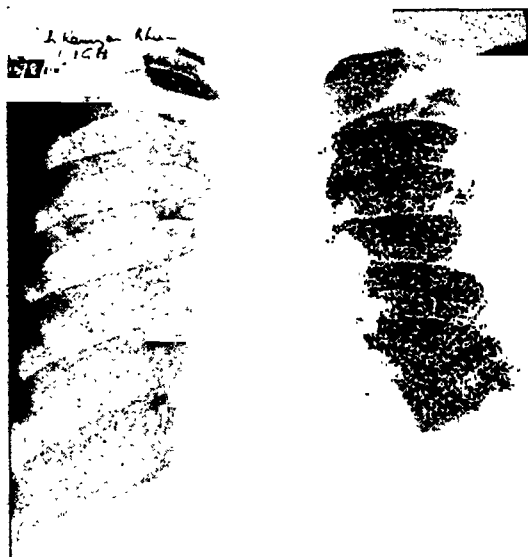


Fig. 1.

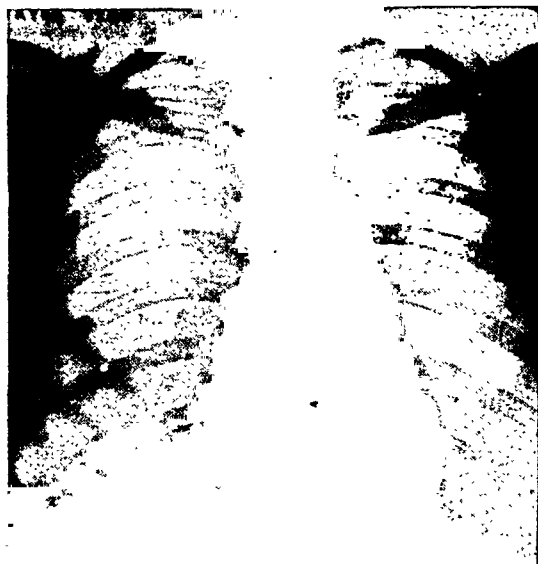


Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.

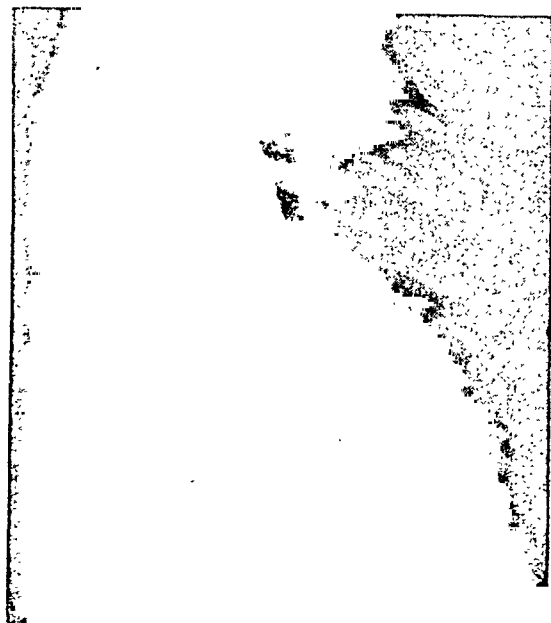


Fig. 6.



Fig. 7.



Fig. 8.



Fig. 9.



Fig. 10.



Fig. 11.

supine position, the inspiratory movements of the diaphragm are ordinarily carried out by the crura and not by the costal attachment. A continued supine position might produce a certain degree of collapse which may be aggravated by irritation of the diaphragmatic pleura near the crura after abdominal operations. While Pasteur and Briscoe emphasized the importance of paralysis of respiratory muscles, Elliot and Dingley (1914) laid great stress on the importance of bronchial obstruction as the chief contributing factor.

A fresh stimulus to the study of massive collapse was given by Bradford (1919) who observed a series of cases of collapse following non-penetrating injuries to the chest during the great war of 1914 to 1918. The chief explanation suggested by him was a reflex paralysis of the respiratory muscles. Those who have observed basal pulmonary collapse associated with infection of a nasal sinus also postulate a reflex nervous stimulus as the causative mechanism. Coryllos and Birnbaum (1928) produced occlusion of the main bronchus by means of an air-inflated balloon which caused pulmonary collapse in six hours. Jacobaeus (1930) noted massive collapse in the human subject within 10 minutes of the introduction of lipiodol.

The most notable contribution to the knowledge of the subject was made by Jackson and Lee (1925) who emphasize the supreme importance of bronchial obstruction in producing atelectasis. Removal of a foreign body in the bronchus is followed by rapid disappearance of collapse. Jackson showed that collapse in diphtheria is not due to paralysis of the diaphragm but to obstruction of the bronchus by membrane and agglutinated mucus. When the obstruction was removed by means of the bronchoscope, the symptoms and signs speedily cleared up. According to him, the cough reflex is the watch dog of the lungs, and when that reflex fails, the lumen becomes completely obstructed. It is interesting to note that as early as 1853, Gairdner gave the three chief causes of pulmonary collapse in infancy as mucus in the bronchi, weakness of the respiratory muscles, and inability to cough.

Hilding (1944), dissatisfied with the explanation of bronchial obstruction, has put forward a fascinating theory based on some convincing experiments by which he has shown that loose mucous plugs can be moved up from the distal to the proximal ends of the bronchi and bronchioles through ciliary action. These mucous plugs act like pistons, and as they move up one after the other, columns of air are removed from the affected lobe until the latter is collapsed completely. The theory is ingenious. It cannot however explain the mechanism of collapse in all cases. His statement that air cannot be absorbed by the blood in the lung capillaries is disproved by the experimental

production of collapse by complete obstruction to a bronchus. In such a case, air could have disappeared from the alveoli only by its being absorbed into the blood stream.

The mechanism of collapse in complete obstruction of the bronchi, either intrabronchial as by foreign body or extrabronchial as by tumour, is easily understood. Air in the obstructed lobe has necessarily to get absorbed into the blood stream. Doubts and difficulties however arise when one tries to work out the process by which portions of the lung become airless in non-penetrating chest injuries, in pulmonary inflammations and after abdominal operations. When the theories so far advanced to explain the pathogenesis of massive atelectasis are analysed, they are found to fall into two broad groups, namely, the bronchial obstruction group and the respiratory paralysis group. Paralysis chiefly of the diaphragm is brought about according to different theories in different ways. It might be a reflex mechanism, or an allergic response, or a true nerve paralysis as in diphtheria. The theory of respiratory paralysis, as the sole cause of atelectasis, cannot be substantiated. Respiratory paralysis no doubt will abolish any movement of air in the alveoli. Air in the alveoli in the natural course of events will be absorbed into the blood stream. It will however be replaced by outside air so long as there is no obstruction in the air passages. Hence, the lung cannot collapse simply as a result of paralysis of the respiratory muscles. Moreover, massive collapse of the lung is not seen to occur after phrenic evulsion. Paralysis of the diaphragm produces only a relaxation of the lung and does not cause all the air in it to disappear. Moreover, neither in post-operative conditions, nor after external chest injuries, do the respiratory muscles get so completely paralysed as to cease functioning. In these conditions only reflex inhibition of respiratory movements occurs and not total abolition. In fact, according to the theory propounded below, a certain amount of respiratory excursion is required to produce pulmonary atelectasis.

The protagonists of the bronchial obstruction theory believe that the complete blocking of the bronchi or bronchioles by thick mucous secretion and the subsequent absorption of air from the alveoli into the blood stream are the processes concerned in the production of atelectasis. It has been seen no doubt that this is the mechanism in case of foreign body obstruction of the bronchi. I am however not convinced that mere mucous secretion, however viscid it may be, can produce complete bronchial or bronchiolar obstruction. Hilding has shown that through the mucociliary mechanism secretion can be moved up the bronchioles. Moreover, a fairly forcible current of air sufficient to dislodge mucous secretion passes to and fro during the process of respiration through the narrow bronchial or bronchiolar passage.

Another point against the theory of complete obstruction is the length of time required to produce atelectasis. In Coryllos' experiment of bronchial occlusion it took nearly six hours to produce atelectasis.

Jacobaeus, on the other hand, observed atelectasis occurring within ten minutes after intra-bronchial instillation of lipiodol. The onset of post-traumatic and post-operative atelectasis is also equally sudden and rapid. It is obvious therefore that the process of absorption of air into the inter-alveolar blood stream cannot explain such a rapid disappearance of air from the lung as occurs in the above-mentioned conditions. What then is the mechanism by which massive atelectasis is produced?

The theory which I wish to put forward as a rational and adequate explanation is substantiated by experiments performed on human body immediately after death and on animal under anaesthesia, as well as by laboratory experiments. I agree with Jacobaeus and Jackson that bronchial or bronchiolar obstruction is a necessary condition to be satisfied before atelectasis occurs. Secretions in the bronchial tubes, both in post-traumatic as well as post-operative conditions, are the obstructing agents. Accumulation of secretion is no doubt caused by diminished respiratory excursion. If the process of rapid disappearance of air from the lung is to be understood, the essential prerequisite of some respiratory movements should be granted. I contend that the mucous secretion in the bronchioles, instead of producing complete obstruction, act like ball-valves allowing air to get out from the lung during expiration but preventing air getting in during inspiration. The ball-valve-like action can readily be conceived because the bronchi are not of the same calibre throughout their length. The distal portions are narrower than the proximal portions. Hence it is easy to imagine how a plug of mucus can effectively block a bronchus or bronchiole as it is moved distally by the inspiratory air current and how, on the other hand, it will allow air to pass through when it is moved towards the broader proximal end. If for instance the lower lobe bronchus is blocked by a mucous plug, some amount of air will be expelled during expiration as a result of the plug being moved to the broader proximal portion of the bronchus and thus rendering it patent. During inspiration, however, air is not allowed to get into the lower lobe which to that extent is partially collapsed. If one hundred cubic centimetres of air get into one lung during each inspiration, all that hundred cubic centimetres of air get into the upper lobe, if the lower lobe bronchus is blocked. During the next expiration, as the inter-alveolar air pressure throughout the chest cavity is higher than the atmospheric pressure, air gets expelled from all the lobes irrespective of the presence or absence of partial collapse. Hence more air passes out from the lower lobe during expiration

without its being replaced during inspiration. With every act of respiration the upper lobe gets more and more collapsed. This process goes on until the lower lobe gets completely airless. The mechanism is facilitated by the inherent tendency of the lung to shrinkage owing to its elasticity. It is quite conceivable how by this process atelectasis can be produced in a few minutes provided there is a ball-valve-like obstruction of the bronchus, and the integrity of respiratory excursion is maintained. Without respiratory movements, a rapid disappearance of air from a partially obstructed lobe cannot be produced. If valvular opening in lung rupture can produce a tension pneumothorax, I don't see any reason why a ball-valve obstruction to the bronchus cannot produce rapid atelectasis. In fact, it is not possible to conceive of any other way by which air can completely disappear from a lobe within the short period of ten minutes or even less. Absorption into the blood stream is out of the question, since it has been shown by Coryllos that it takes nearly six hours for atelectasis to be produced by complete obstruction during which air is absorbed into the blood.

Even the presence of liquid secretion in the bronchiole under favourable circumstances will contribute to the establishment of 'one-way traffic' for the air, which might bubble out through the fluid during expiration, but will not be allowed to get into the affected alveoli during inspiration. This is facilitated by the decreasing calibre of the distal portions of the bronchi and bronchioles. Each of them is in the shape of a more or less narrow conical tube. If it contains fluid secretion, the air from the alveoli attached to its narrow end can bubble through, but air coming from outside through the proximal end will not be allowed to pass as the fluid will be driven to the narrow distal end where it will form an effective block for the air. In the case of multiple lobular atelectasis after drowning described previously by the writer (1941), sea water acted as the obstructing medium and evidently operated by the above-described mechanism. It is obvious that not only should there be an obstructing agent in the respiratory passages but the respiratory movements should be maintained as well.

The following experiments were performed to substantiate the theory described above:

Experiment 1.—The first experiment was on a human body immediately after death. Materials required had been got ready previously as the time of death was anticipated. The trachea was opened into and a rubber tube was introduced into the right bronchus. Twenty cubic centimetres of an oil emulsion of the consistency of lipiodol were introduced through the tube. Artificial respiration by the writer's method (1945) was given for five minutes. The trachea was then plugged air tight with a cork. The chest was opened in the usual manner. The

right lower lobe was found to be distinctly, though partially collapsed (see figure 6), while the left lung and right upper lobes remained distended owing to the trachea being plugged.

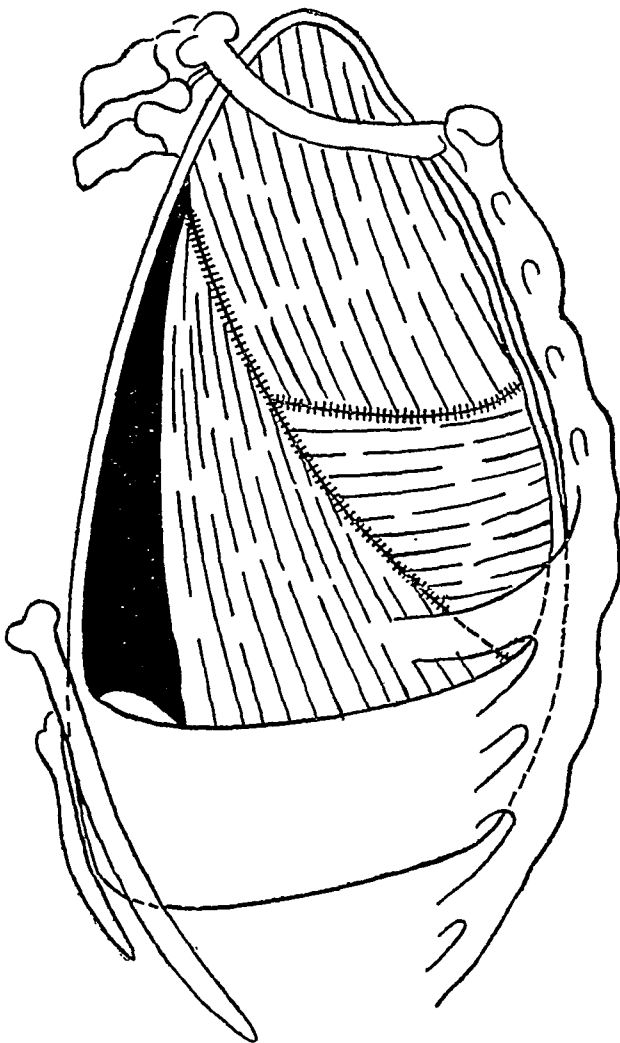


Fig. 6.—Lateral view of the chest showing lobar divisions of the right lung. Darkened area represents the position, shape and situation of the lower lobe when collapsed.

Evidently the emulsion had gone into the right lower lobe bronchus and produced the necessary block. With the help of artificial respiration and blockage of the bronchus, collapse of the lower lobe was obtained.

Keeping the thoracic structures *in situ*, the left bronchus was opened into, and two rubber tubes were introduced into the upper and lower lobe bronchi. They were pushed in so as to make them fixed inside. The free ends of the tubes were connected to the bifurcated ends of a Y-shaped nozzle whose opposite end was connected to the exit end of a Higginson's syringe. Air was pumped in to make the lobes partially distended. The tube to the lower lobe bronchus was disconnected from the nozzle, and after a few cubic centimetres of soft-soap emulsion had been introduced, it was reconnected. Air was pumped in with the aid of the

syringe. It was found that while the upper lobe was getting distended, the lower lobe remained as it was. The Higginson's syringe was disconnected and a uniform pressure was applied to both the lobes. Both the lobes collapsed. When air was pumped in further, the upper lobe alone expanded, while the lower lobe remained collapsed, occupying a posterior position in the chest cavity (see figure 7).

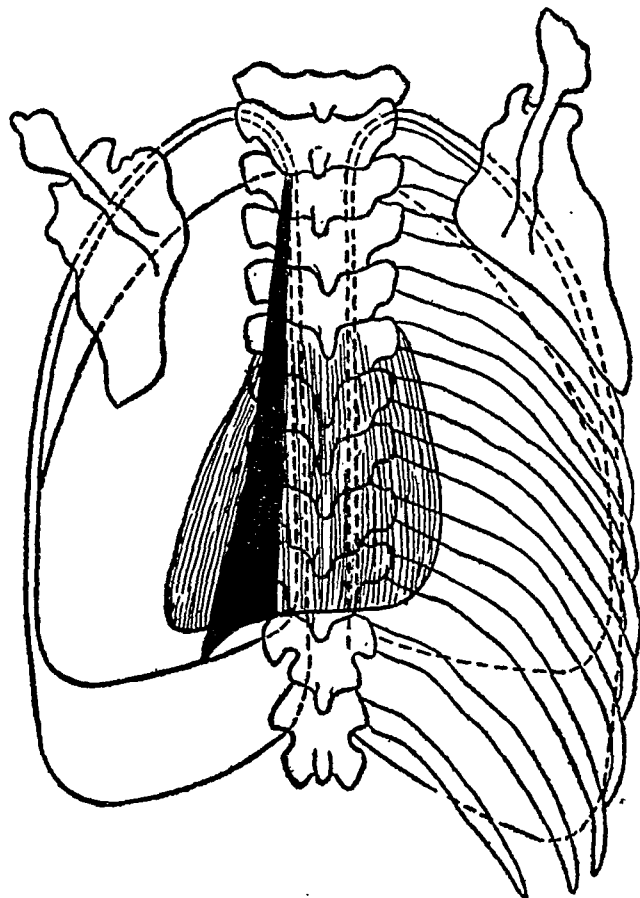


Fig. 7.—Back view of the chest. The darkened triangular area superimposed on the heart shadow represents the collapsed left lower lobe.

Experiment 2.—A simple laboratory experiment was designed to show the mechanical nature of the process involved in the production of atelectasis. A large wide-mouthed jar with a narrow opening at the side but near the bottom was chosen. It was fitted with a cork with two perforations through which two glass tubes were introduced. Each tube tapered to a capillary end. A small football bladder was fitted to each of the tubes so that the bladders remained suspended inside the jar. The lower opening in the jar was closed with a cork to which a glass tube was fitted (see figure 8). The outer end of the glass tube was connected to a rubber tubing to the free end of which was fitted the lateral nozzle of a Potain's aspirator. The air from the jar was aspirated to such an extent as to produce moderate distension of the bladders. The aspirator was then removed and the nozzle of an ear syringe was fitted to the rubber tube. By working the piston to and

fro, a bellows action could be produced so as to increase or decrease the pressure of air inside the jar to an equal measure each time. The result was, the bladders contracted or expanded as the pressure of the air inside the jar increased or decreased. The jar represented the chest and the bladder represented two lobes of a lung. The glass tubes fitted to the bladders represented the bronchi.

Into one of the glass tubes was introduced a small mucous plug from the sputum of a patient. The syringe was worked slowly at the rate of eighteen per minute. It was found

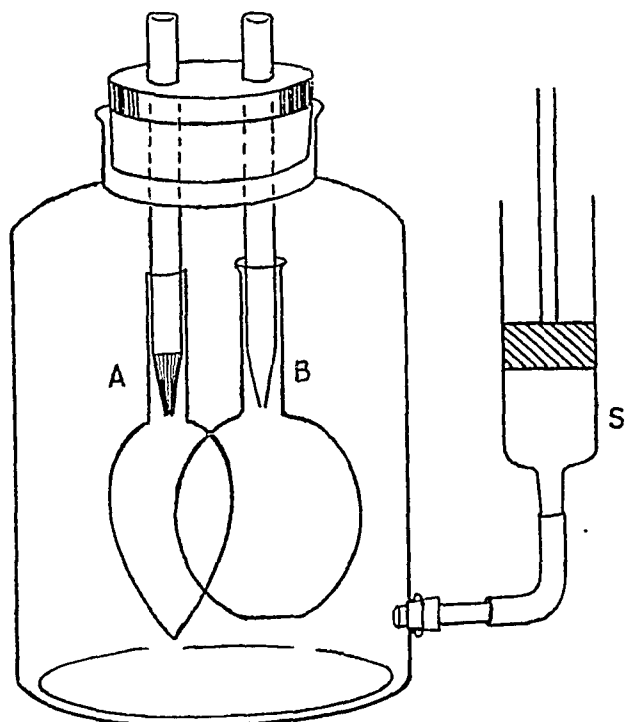


Fig. 8.—Pulmonary atelectasis laboratory experiment 2. Figure represents the state of the bladders at the termination of the experiment. Note 'A' in which the bladder is collapsed owing to presence of secretion in the glass tube. In 'B' the bladder is distended as there is no obstruction. 'S' represents the syringe.

that the bladder connected to the glass tube into which the mucous plug was introduced contracted each time when air was pumped into the jar but failed to expand when the process was reversed. The result was that the bladder shrank in size, and as it shrank the other bladder expanded more and more.

The experiment was repeated with a viscid fluid inside one of the glass tubes. It was not successful as it was found that the fluid was gradually getting aspirated into the bladder through the capillary opening. The tubes being vertical, action of gravity helped in driving the fluid through. In order to overcome this difficulty the jar was kept slanting about 5° from the horizontal. This would have more or less corresponded to the recumbent position of a patient in bed. As the action of gravity was almost overcome in this manner, the experi-

ment succeeded. The air from the bladder bubbled out through the fluid during the process of contraction. The fluid however effectively blocked the passage of air back into the bladder. The same results as in the experiment with mucous plug were obtained.

It has been conclusively proved by the above experiments that obstruction to the bronchi either with semi-solid or fluid material, recumbent posture and shallow respiration are the necessary and sufficient conditions to produce atelectasis of the lung.

Experiment 3.—A dog was anaesthetized. Chloroform was used so as to produce shallow respiration. The trachea was opened into at the lowest possible level and a rubber catheter was introduced into the right bronchus, ten cubic centimetres of viscid sputum were introduced through the catheter. The dog was kept under, for another ten minutes, during which period shallow respiration was maintained. The dog was killed by deepening the anaesthesia. The trachea was firmly plugged with a cork so as to allow no air to escape from the lungs consequent on their shrinking during the opening of the chest cavity. On post mortem, it was found that the lower lobe of the right lung was almost completely collapsed.

All the experiments described above conclusively substantiate the theory propounded in this paper. The pathogenesis of atelectasis can be briefly summarized as follows: Taking post-operative atelectasis as an example, the process starts with the accumulation of secretion in the bronchi and/or bronchioles. This is facilitated by diminished respiratory movements and temporary dysfunction of the mucociliary mechanism. Owing to progressive distal narrowing of the bronchioles, the secretion effectively prevents the air getting into the alveoli during inspiration, but allows it to escape outside during expiration. This process therefore depends on the integrity of the respiratory movements however shallow they might be. After repeated acts of respiration the affected lobe gets collapsed.

Apart from post-anaesthetic conditions, restriction of respiratory movements can be produced through pain, either pleuritic or post-traumatic. Excessive secretion necessary for blockage can be produced either by bronchiolar inflammation as in the first case, or by post-traumatic hæmorrhage as in the second. The mode of production of atelectasis in the third case was similar to that in Coryllos' experiment, namely, complete bronchial obstruction and subsequent absorption of air into the blood stream. The more frequent occurrence of lower lobe atelectasis, particularly in post-operative conditions, is due to several factors. The whole of the posterior surface of the lower lobe (see figure 6) is in contact with the back of the chest and practically the whole of the diaphragmatic surface of the lung is formed by the lower lobe. When the back is fixed in the

recumbent position, if the diaphragmatic movement also is restricted either through post-anæsthetic shallow breathing or through tight abdominal bandaging, the respiratory excursions of the lower lobe will be rendered relatively smaller than that of the upper lobe. Hence stasis of secretion occurs more easily in the lower lobe bronchioles. Moreover the lie, direction and inclination of the lower lobe bronchus and its branches are more favourable to the production of a ball-valve action of the secretion inside them. Lower lobe atelectasis is therefore less likely to happen if the patient after operation is propped up or turned to one side. Perhaps by keeping the patient in the Trendelenburg position until normal breathing is established, pulmonary atelectasis might be prevented, as it will prevent accumulation of secretion in the lower reaches of the bronchioles.

Summary

(1) Three cases of lower lobe atelectasis are described.

(2) A short review is given of the available literature on the pathogenesis of atelectasis.

(3) The opinion is expressed that the establishment of 'one-way traffic' for the air in the bronchioles by the ball-valve action of secretion inside is the cause of pulmonary atelectasis. Respiratory movements are none the less necessary.

(4) Experiments are described to substantiate the theory.

(5) Reasons for relative frequency of lower lobe atelectasis are cited.

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MEDIASTINAL EMPHYSEMA

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THE total number of cases of spontaneous mediastinal emphysema reported so far is 23; of these, 22 cases were reported by Hamman (1934), but none of these 22 cases was admitted to hospital unconscious and with high temperature. The following case report will therefore be of interest :—

A male, aged 45 years, was admitted to hospital unconscious, restless and dyspnoic on the 4th May,

1945. There was a generalized erythematous blush of the skin over the face, neck and chest. The skin on palpation gave a distinct feeling of crepitus. The temperature was 102°F.

History.—The patient, an average individual with well-developed musculature, was apparently in good health and had never suffered from any chronic cough. Three days before admission he was out fishing on a boat, and suddenly developed fever with pain in the chest, particularly marked in the precordial region. There was no history of constipation, drowsiness, vomiting, headache, convulsions, twitching, fits or paralysis, or addiction to alcohol. He did not complain of any acute pain in the head before losing consciousness such as is seen in profound shock.

Clinical examination.—On pinching the skin on the back of the hand it was withdrawn; on stimulation there was voluntary movement. The corneal reflexes were present. The pupils were equal and dilated and reacted to light. Examination of the fundus oculi showed slight blurring of the disc and congestion of the retinal vessels. The ocular tension was normal. There was no rigidity of the neck; the neck veins were found congested.

The temperature continued from the onset of fever and shot up to 104.8°F. within half an hour of admission. The pulse rate was about 130 to 140 per minute; the pulse was full, rapid and easily compressible. The respiration rate was about 40 per minute. The blood pressure was 125/65.

The apex beat could not be palpated properly owing to surgical emphysema. On percussion, the normal area of cardiac dullness was found obliterated and the note was particularly hyper-resonant. There was a rough, to and fro, grating sound heard anteriorly from the left margin in the 4th and 5th intercostal spaces up to half an inch internal to the mid-clavicular line.

The breathing was hurried but not stertorous or irregular; the breath sounds could not be heard distinctly and were diminished. The percussion note was resonant. Crepitus could be felt from the temple down to the upper half of the abdomen. The nasal sinuses were congested. The upper abdomen was prominent and on palpation gave a distinctive crepitus. The spleen and liver could not be palpated.

The lips were cyanosed, the tongue was red, and the throat congested; a slough was seen over the tonsil; the slough was removed easily and sent for bacteriological examination. Both tonsils were inflamed.

There was no hemiplegia or hemiparesis. Tendon reflexes were sluggish.

Laboratory examinations.—Blood examination showed moderate anæmia (hæmoglobin 60 per cent) and some polymorphonuclear leucocytosis. No malaria parasites were found. Blood culture was sterile. Urine was normal. Friedlander's pneumobacilli were isolated from culture of the throat swab. Lumbar puncture showed the cerebro-spinal fluid under some pressure but clear in general appearance.

Treatment.—Morphine and atropine injections were given immediately on admission, and penicillin 20,000 units immediately and 15,000 units every three hours for 6 days, the daily dose being 100,000 units. An alkaline mixture was given thrice daily and glucose injections twice daily.

For the first two days no food could be given orally. Fluid diet was given from the third day, and soft rice and fish from the 11th day.

Course and prognosis.—The patient's fever continued varying from 99°F. to 102°F. for more than a week (see temperature chart). His general condition was grave for two days, during which period he was unconscious. He became conscious on the third day of admission and talked sensibly; but the temperature and the condition of surgical emphysema persisted, as also the sound in the cardiac area. A few râles and crepitations were heard at the bases of the lungs.

The temperature came down to normal on the 14th day. Crepitus disappeared first from the face, then from

[illegible]

there was no abnormal sound in the heart or lung, and the apical impulse was in the 5th intercostal space half an inch internal to the mid-clavicular line. The case was followed up for two months after discharge, and the heart and lungs were found to be normal.

The skin all over the body from the temple to the upper half of the abdomen was elevated and the crepitus was so evident that the case was at once diagnosed as interstitial emphysema. The cause for such a condition, in the absence of any history of injury, operative procedure or previous tuberculosis, and with the high temperature and unconsciousness, was not so easy to detect. The blood examination showed no malaria parasites, and it is impossible to explain surgical emphysema by a malignant tertiary infection. The sudden onset of fever and hyperæmia of the mucosa of the nose and mouth and the raised pulse rate might suggest influenza, but the course of fever was long and there was no leucopenia. The history of the case, the physical examination and the laboratory tests do not suggest any cerebrovascular lesion or uræmia or diabetes as the cause of coma.

The high temperature with rapid pulse and respiration was suggestive of streptococcal infection from the throat, the toxins affecting the brain and causing unconsciousness till the infection was brought under control by penicillin treatment. The streptococcal infection causing congestion of the lung was possibly responsible for the rupture of the pulmonary alveoli; the skiagram of the chest (*see figure 1, plate IV*) shows an air track arising from the root of the right lung, escaping upwards along the bronchi and the blood vessels into the mediastinum, and passing up to the subcutaneous tissues of the neck.

simulate coronary thrombosis or pericarditis. Hamman described the physical signs as a peculiar cracking bubbling sound heard over the heart with each contraction, not lasting long. The case under report showed the same physical signs as described by Hamman but the signs persisted for more than two weeks.

I express my grateful thanks to Lieut.-Colonel R. Linton, I.M.S., Principal, Medical College, Calcutta, for allowing me to make use of the hospital records and to report this case.

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S. B. SHAH, M.S. (Bom.)

THE abnormality was discovered accidentally when the patient came to a dispensary in Ahmedabad for treatment of a small ulcer on his left leg.

Clinical findings.—The patient is a male, aged about 20. His general appearance is healthy for his age (figure 1, plate IV), and the mental development is in conformity with his social status and education. He comes from Nagpur.

In the right arm the lower end of the humerus cannot be distinctly made out though the two epicondyles can be felt: the medial condyle is unusually prominent. There is no elbow joint. A single bone, probably representing both the radius and ulna and only $2\frac{1}{2}$ inches long, is attached to the lower end of the humerus by a synostosis. The wrist joint also appears to be missing. In the palm which is small and oblong, two metacarpals can be felt. The thumb is absent and only two fingers are seen. It is not possible to say which fingers these are. The total length of the arm is 19 inches, that of the humerus being $11\frac{1}{2}$ inches.

In the left arm the lower end of the humerus projects as a point. At about 8 inches from the acromion, a mass is seen attached laterally to the humerus. This mass represents the wrist joint, the palm and two digits, one of which appears to be the thumb. The forearm and elbow joint appear to be completely absent. The humerus is shorter than its fellow, being $10\frac{1}{2}$ inches long.

In spite of the handicap, the patient can feed himself, clothe himself and wash himself. He can pick up a coin from the floor and lift a bucketful of water.

No other abnormality is seen in any other part of the body except that the forehead is rather sloping, and the frontal and parietal eminences are not felt.

Radiological findings (figure 2, plate IV).—Right superior extremity, lateral and antero-posterior views show two projections simulating two epicondyles, and a long projection about $2\frac{1}{4}$ inches long appearing like the lower end of the radius. The medial epicondyle is unusually prominent. The carpal bones consist of four bones which appear to represent the lunate, triquetral, the pisiform and a fused mass representing the rest. Two complete fingers with their metacarpals are seen and are normal.

The elbow joint is absent; the wrist joint is present; and also the carpo-metacarpal, metacarpophalangeal and the interphalangeal joints.

The left superior extremity shows a bone which represents an ulna joined to the humerus, both being undefined. The carpal bones are represented by two bones, the proximal and distal rows. Two metacarpal bones are seen and the outer one has only one phalanx whereas the inner one has two phalanges attached.

Comments.—As the condition is bilateral, we are inclined to believe that it is hereditary, though there is no history of any such case among the patient's brothers and sisters nor in either of his parents. His father is dead and his mother is far away and not available for interview. In any case, family histories in India are always difficult to elicit and notoriously unreliable.

Perkins (1936) states as follows:

'The foetal limb bud consists of: (1) a root segment near the trunk, (2) an intermediate segment which separates into two parallel segments, and (3) a terminal segment which separates into five parallel segments. Abnormalities may occur in the growth of the limb buds, resulting in suppression, hypoplasia or hypertrophy; and abnormalities may occur in the segmentation of the limb buds, resulting in either the production of supernumerary segments, or a fusion of segments. Fusion between the root segment and the intermediate segment is rare; more commonly one of the intermediate segments is fused with its fellow, e.g. radio-ulnar synostosis; most common of all, two of the terminal segments are fused together.'

Our case represents both a fusion, that of the humerus with either the radius or the ulna (if our surmise is correct), and a suppression of some carpal bones, many metacarpals and phalanges.

In the view of one of us (K. A. S.), the deformity of the hands is a variety of split-hand or lobster-claw, which is usually due to a dominant gene. It was this fact which induced him to study and investigate the case but the attempt to find sufficient data has not been successful.

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ANALYSIS OF 242 CASES OF SPRUE IN INDIAN TROOPS*

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A CONDITION manifesting itself in various degrees of emaciation accompanied by diarrhoea, indigestion, glossitis and anæmia, has of late been described under the labels of parasprue (Chaudhuri and Rai Chaudhuri, 1944), nutritional diarrhoea (Karamchandani, 1944), incomplete sprue (Manson-Bahr, 1940), chronic jejuno-ileal insufficiency (Bennett and Hardwick, 1940), and vitamin B deficiency syndrome allied to sprue (Cook, 1944). Rogers (Rogers and Megaw, 1942) is of the view that unexplained diarrhoea of more than 10 days' duration should be treated as sprue, provided amebic disease is excluded. We are in agreement with the last view; it is not necessary that the whole picture with glossitis, flatulent dyspepsia, fatty diarrhoea containing high percentage of split fat, emaciation and macrocytic anæmia must be complete before the label of sprue should be applied.

Pathology.—In this syndrome, with faulty intake and faulty absorption, the stress initially falls on the delicate columnar epithelium of the intestines and the symptoms depend upon the site and extent of stress. Thus (A) when the duodeno-jejunal region is affected there may be deficiency of bile flow which means fat not emulsified, i.e. fat even when split is not absorbed, hence increase in split fat; or, deficiency of pancreatic secretion, and consequently deficiency of splitting of fats and high total fat content in the stools; or, when both bile flow and pancreatic secretion become deficient, typical white sprue stools occur with great increase in fat. (B) When the ileum is affected, the fat content in stools is normal and the diarrhoea is predominantly of an irritative kind (enteritis). (C) When the colonic area is affected, mucus and even blood are found in the stools (colitis).

The next stage in the stress comes when, in addition to the affection of the delicate columnar epithelium, increased vascular permeability occurs. In the stomach, irritative gastritis is produced, and this is responsible for rapidly developing anæmias and in the intestines, diarrhoea is accentuated.

In the third stage infection is superimposed. These infections are salmonellas in the small intestines and not of importance; but in the large intestines, amebic infection shows concomitant chronic intoxications and bacillary infection shows ulcerative colitis, with rapid intoxication. At this stage, fatty diarrhoea, with progressive and rapid asthenia and anæmia is found.

Finally, complication may extend to the nervous mechanism. These changes when confined to the more superficial Meissner's plexuses manifest themselves in accentuation of the secretory variety of diarrhoea, the villi pouring out watery diarrhoea (easily controlled by chlorodyne); when extending deeper into the Auerbach's plexuses, the motor accentuation with hypermotility of lenteric variety occurs which accentuates mal-absorption and increase of split fat in stools.

The post-mortem findings in two typical cases are given.

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Case 1.—Small intestines wasted, destruction of villi with thinning and wasting of mucous membrane. Large intestines atrophied, liver atrophied; kidney cloudy swelling; suprarenal glands atrophied.

Histopathological report: jejunum—thinning of mucosa, incomplete destruction and shrinkage of villi with loss of epithelia and its secretory glands. Fibrosis and necrosis of sub-mucosa with round cell infiltration.

*Case 2.**—The whole of the ileum was diaphanous in appearance, but inadvertently only sections from the colon were sent for histopathological examination.

Mucosa shows desquamation of epithelial cells together with necrosis, the small ulceration being limited as far as sub-mucosa. Sub-mucosa markedly oedematous; blood vessels are dilated with extravasation in the core of villus-like processes; perivascular round cell infiltration present. Muscularis oedematous, more marked in the intermuscular plane; very little inflammatory reaction noticed. Serosa unaffected.

A series of 242 cases of the sprue syndrome was observed in this hospital during a period of 2½ years. All these patients had returned from campaigns and were treated on the lines laid down at the specialists' conference (Karamchandani, 1944). These 242 cases were grouped according to their predominant symptoms as follows: dyspepsia and diarrhoea, 88 cases; dyspepsia, diarrhoea and glossitis, 96 cases; dyspepsia, diarrhoea, glossitis and anæmia, 54 cases; dyspepsia, diarrhoea, glossitis, anæmia, and excessive split fat in stools, 4 cases. Table I gives the detailed analysis of these four groups.

of the number in groups, while the cure rate ran in the opposite direction, that caste played no special rôle, that the majority of stools were of clay colour, liquid consistency, and frothy appearance, and that although 31 cases had amœbic infection as reported by the laboratory, only 6 had blood and mucus in the stools.

Treatment.—During the first 3 days, the diet consisted of 8 oz. of milk, given every 2 hours from 6 a.m. to 10 p.m. This was increased to 10 oz. during the next 4 days; the increase was gradual and subject to variety in the forms of sprue tea (tea infused in milk), ovaltine, and Horlicks milk. This diet provided a caloric value 1625, with 82 gm. protein, 90 gm. fat and 120 gm. carbohydrate. During the second and third weeks the diet was scheduled as diet no. 1 (see appendix), providing 2560 calories with 97, 70 and 458 gm. of protein, fat and carbohydrate respectively. During the next three weeks the diet was augmented to no. 2 (see appendix), providing 3200 calories with 154, 114 and 596 gm. of protein, fat and carbohydrate, respectively. Vitamins were provided for as follows: raw liver juice, extracted from 8 oz. of liver and flavoured with lime juice, administered in a coloured glass container. When available, injections of liver extract were given to cases with anæmia according to the Reserve Depot line of

TABLE I
Analysis of symptoms in 242 cases of sprue

Group number	Hindu	Muslim	Others	AGE, YEARS			Average duration, months	Number of stools in 24 hours	Stools							Gastric acid curve	BLOOD PICTURE			
				20-25	25-30	Over 30			Colour			Consistency		Abnormalities			Normal, %	Macrocytic, %	Microcytic, %	
									Clay	Brownish	Yellow	Watery	Pultaceous	Gas	Blood and					Amoebiasis
I	53	35	..	61	27	..	6½	4	63	10	15	52	36	8	8 cases done, all normal. 20 cases done, normal 85%, achlorhydria 15%. 24 cases done, normal 79.1%, achlorhydria 20.9%. 1 case done, normal.	86.4	10.2	2.4
II	62	30	4	72	18	6	7½	6	82	12	2	62	33	14	3	12		79.2	15.6	5.2
III	32	22	..	40	12	2	8	8	32	13	9	44	10	18	3	19		59.2	26.0	14.8
IV	2	2	..	2	1	1	6	15	4	4	..	2	100.0	..

It will be seen from table I that the majority of cases fall within the ages of 20 and 25 years, that the duration of the disease had no bearing on its severity, that the deterioration in the blood picture and increase in the frequency of stools ran parallel with the advance

treatment, i.e. 8 c.cm. of crude extract to begin with and 4 c.cm. every alternate day till six injections. Vegemite ½ oz. twice a day, flavoured with 25 c.cm. of essence of chicken and diluted with hot water to taste. Orange juice 2 oz. containing M xx of diluted hydrochloric acid. In special cases nicotinic acid and ascorbic acid tablets were given. Calcium lactate and chlo-rodylene were also found useful.

*Not included in this series, but quoted from Karamchandani, 1944.

Those with concomitant amoebic infection were given routine army treatment which consisted of emetine parenterally for 6 days, retention enema (8 oz. of 2½ per cent yatren) from the 5th to the 14th day, emetine bismuth iodide 3 gr. orally from the 7th to the 12th day, and amœbiarson 1 tablet (0.25 gm.) twice a day from the 13th to the 25th day.

After six weeks' treatment every case was given one month's leave. The patients were then disposed of under three classes: (a) duty; (b) categorized 'C' permanent, i.e. fit for duty in India only, with no parade and P. T.; and (c) categorized 'E' invalidment. These were examined at intervals and the relapses invalided. The results of treatment are given in table II.

TABLE II
Analysis of results

Cured, discharged to duty ..	129	(53.4%)
Improved, categorized 'C' permanent.	22	(9.0%)
Improved, categorized 'C' permanent and relapsed—therefore invalided out of service.	67	(36.8%)
Not improved and invalided out of service.	22	
Died	2	(0.8%)
	242	(100.0%)

Acknowledgment

Grateful recognition is given of valuable assistance by my colleague Major K. Bannerji, Dist. Pathologist.

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APPENDIX

Time	Diet No. 1. 2nd and 3rd weeks	Diet No. 2. 4th to 6th weeks
0600 hours	Sprue tea (i.e. milk tea), 8 oz.	Sprue tea (i.e. milk tea), 8 oz.
0800 "	Milk 8 oz., toast 2 oz., eggs 2.	Milk 8 oz., toast 2 oz., eggs 2.
1000 "	Milk 8 oz., vegetables 2 oz., vegemite ½ oz.	Milk 8 oz., vegetables 4 oz., vegemite ½ oz.
1200 "	Milk 8 oz., toast 2 oz., juice from 8 oz. liver.	Milk 8 oz., toast 2 oz., juice from 8 oz. liver.
1400 "	Kher 6 oz., or rice 4 oz. with milk or porridge 8 oz.	Kher 6 oz., or rice 4 oz. with milk or porridge 8 oz.
1500 "	Fruit juice 6 oz.	minced meat 4 oz. Fruit juice 6 oz.

APPENDIX—concl'd.

Time	Diet No. 1. 2nd and 3rd weeks	Diet No. 2. 4th to 6th weeks
1600 hours	Milk 8 oz., tea.	Milk tea 8 oz., toast 2 oz.
1800 "	Milk 8 oz., toast 2 oz., juice from 8 oz. liver, khichri 4 oz.	Milk 8 oz., toast 2 oz., juice from 8 oz. liver, khichri 4 oz.
2000 "	Milk 8 oz. with Horlicks.	Milk 8 oz., chicken soup ½ pints.
2200 "	Milk 8 oz., vegemite ½ oz.	Milk 8 oz., vegemite ½ oz.

Lassi of dahi 2 lb. between 0900 to 1600 hours.
Lemon water 2 pints when required.

ON THE TOXICITY OF SOME ORGANIC ANTIMONIAL DRUGS USED FOR THE TREATMENT OF KALA-AZAR

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DERIVATIVES of antimony have proved very useful remedies in the treatment of both schistosomiasis (bilharziasis) and leishmaniasis (particularly kala-azar). Both these diseases are widespread. Some indication of the value of antimony is the fact that without treatment the death rate from kala-azar is over 90 per cent, whereas with treatment in Indian kala-azar it is reduced to below 10 per cent.

Although tartar emetic was found of value in the treatment of kala-azar, its considerable toxic effects made it imperative to obtain other derivatives which should be better tolerated while having, if possible, a greater therapeutic effect. The introduction of a pentavalent organic antimony derivative, urea stibamine, by Brahmachari in the year 1922, was an important development in the history of chemotherapy of kala-azar. Urea stibamine is obtained by the interaction of *p*-aminophenylstibinic acid with urea. The exact chemical nature of this important drug is still not definitely known. Since its discovery, attempts have been made by various workers in different laboratories to produce an ideal drug for the treatment of kala-azar. Most of the organo-antimonials that have had clinical trials have been derivatives of *p*-aminophenylstibinic acid. Besides urea stibamine, neostibosan (the diethylamine salt of *p*-aminophenylstibinic acid) has also proved effective in the treatment of kala-azar.

The carbon-to-antimony bond in organic antimonials is much weaker than the analogous carbon-to-arsenic bond and, as a result, many antimonials tend to decompose in solution. Because of the nature of antimony chemistry, the factors affecting administration, absorption

and toxicity are important. Moreover, the preparation of these compounds in commercial quantities is difficult, as evidenced by the many reports of variations between samples of the same compound. In kala-azar, secondary effects are very undesirable owing to the much longer period of treatment. Urea stibamine, although a very potent drug for the treatment of kala-azar, has been reported to show at times toxic reactions. The cause of such toxic manifestations deserves further investigation.

It is not known exactly what determines the toxicity of organic pentavalent antimony compounds. It is surmised that, in the body, the pentavalent forms slowly decompose into trivalent antimony compounds, which ultimately produce the therapeutic action of the drugs. It has been frequently observed that different batches of the same antimony preparation, though prepared under apparently identical conditions, differ markedly in their toxicity. Moreover, the different derivatives of *p*-aminophenylstibinic acid also vary widely in their toxicity. It has been, therefore, considered to be of considerable interest to study the properties of some derivatives of *p*-aminophenylstibinic acid, with a view to ascertaining the factors underlying the development of their toxicity.

The present communication deals with a study on the toxicity of some derivatives of *p*-aminophenylstibinic acid in relation to their antimony contents. The recorded data are collected from the results of experiments with some of the typical samples, though the conclusions are based essentially on the analyses of more than a hundred samples of urea stibamine and other derivatives.

Experimental

Study on the toxicity of urea stibamine.—Our first object was to study the influence of the total antimony content on the toxicity of urea stibamine. For this purpose, several batches of the drug (primarily prepared in this laboratory, and a few samples obtained from the market) have been subjected to acute toxicity tests and chemical analyses with regard to total antimony contents. With some samples (*, *vide* table I), the antimony content was artificially lowered by mixing mechanically with some quantity of anhydrous glucose, in order to find the effect of the lowering of the antimony content on the production of toxicity. All the toxicity tests were carried out on white mice (weight varying from 14 to 16 grammes), according to the procedure described by Burn. Observations of mortality were made up to a period of 96 hours. The total antimony content was determined according to the method of Gray (1926). All these results are summarized in table I. Samples (1 to 10) were prepared in this laboratory and samples (11 and 12) were obtained from the market.

Samples were dried at ordinary temperature in a vacuum desiccator over fused calcium chloride till the weight was constant.

TABLE I
Toxicity of different samples of urea stibamine of different antimony content

Sample number	Total antimony content, per cent	Intravenous dose of the drug, mg./kg.	Reaction in 30 minutes	Mortality in 96 hours among 10 white mice
1	41.3	250	Slight	0
2	38.5	250	"	2
3	42.0	225	Severe	6
*3a	35.0	225	"	4
4	43.6	225	"	8
*4a	39.0	225	"	6
5	40.2	225	"	4
6	29.9	225	Moderately severe.	6
7	26.0	225	"	6
8	20.0	250	Slight	0
9	20.1	250	Severe	3
10	41.9	275	Moderate	1
11	40.3	225	Severe	5
12	40.0	225	"	4

The above results indicate that the toxicity of urea stibamine does not depend solely upon the total antimony content. Even with an appreciably low antimony content, a sample may possess undue toxicity.

It is, however, known that antimonious and antimonious acids are formed, though in small quantities, during the preparation of urea stibamine. In order to see if the presence of these acids has any influence on the production of toxicity, the antimony content (in various states, such as the inorganic state or in organic combination, trivalent or pentavalent) of some samples were estimated. These estimations have been carried out according to the method of Gray (1926) and other standard methods as quoted by Datta, Ghosh and Bose (1945), a blank experiment having been carried out in each case. The antimony content present in organic combination in the pentavalent state was deduced by subtracting the percentage of antimony (present as antimonious acid) from that of total antimony content present in the pentavalent state. The results obtained are summarized in table II. This table indicates that toxicity is related to the amount of antimonious acid present.

Acute toxicity of other pentavalent organic antimony compounds

In order to have an idea of the toxicity of other pentavalent organic antimony compounds in comparison with that of urea stibamine, several samples of the diethylamine salt and of tri-*iso*-propylamine salt of *p*-aminophenylstibinic acid, prepared in this laboratory (compare Ghosh, Bose and Mitra, 1945), have been

TABLE II
Toxicity of urea stibamine and the state of the antimony

Sample number	PERCENTAGE OF ANTIMONY					Intravenous dose of the drug mg./kg.	Mortality in 96 hours among 10 white mice	Ratio of (c) : (e)
	Total (a)	Total pentavalent (b)	Present as antimonious acid (c)	Present as antimonic acid (d)	In pentavalent organic combination (e)			
1	39.4	38.2	1.15	1.05	37.15	225	1	1 : 32.3
2	40.2	39.34	0.88	1.08	38.26	225	0	1 : 43.4
3	42.5	41.04	1.5	1.2	39.84	225	2	1 : 26.5
4	38.4	36.2	2.3	1.3	34.9	225	4	1 : 15.1
5	34.9	33.0	2.1	1.25	31.75	225	3	1 : 15.1
6	40.4	38.0	2.5	1.5	36.5	225	4	1 : 14.6
7	36.0	33.1	2.86	1.6	31.5	225	4	1 : 11.0
8	37.5	36.5	1.02	1.01	35.49	225	0	1 : 34.7
9	41.8	40.91	0.92	1.3	39.61	225	1	1 : 43.0
10	39.8	38.8	1.05	1.1	37.7	225	1	1 : 35.9

TABLE III

Samples prepared in this laboratory were dried in a vacuum desiccator over fused calcium chloride till the weight was constant

Amine used	Sample number	Percentage of total antimony	Dose of the drug mg./kg.	Mode of administration	Reaction in 30 minutes	Mortality in 96 hours among 10 white mice
Diethylamine, manufactured by Schering-Kahlbaum (obtained in sealed tubes).	1	42.5	250	Intravenous	Severe	10
	2	42.5	250	"	"	6
	2	42.5	300	Subcutaneous	Slight	3
	2	42.5	350	"	Severe	10
	3	43.6	300	"	"	10
Diethylamine, from Schering-Kahlbaum, once distilled here.	4	42.1	250	Intravenous	Moderate	1
	4	42.1	300	"	Severe	2
	4	42.1	300	Subcutaneous	Nil	0
	4	42.1	350	"	Moderate	2
	4	42.1	400	"	Severe	4
Diethylamine, from Schering-Kahlbaum, thrice distilled here.	5	42.1	300	Intravenous	Moderate	0
	5	42.1	350	Subcutaneous	Nil	0
	5	42.1	400	"	Nil	0
	6	41.8	400	"	Nil	0
	6	41.8	300	Intravenous	Nil	0
Bayer's neostibosan	7	42.1	250	"	Nil	0
	7	42.1	300	"	Nil	0
	7	42.1	300	Subcutaneous	Nil	0
	7	42.1	350	"	Nil	1
	7	42.1	400	"	Nil	1
Tri-iso-propylamine, manufactured by Eastman Kodak Co.	8	36.3	350	"	Moderate	6
	9	36.5	350	"	"	5
Tri-iso-propylamine, from Eastman Kodak Co., thrice distilled under reduced pressure.	10	36.7	300	Intravenous	Moderate	0
	10	36.7	350	"	Severe	4
	10	36.7	350	Subcutaneous	Nil	0
	10	36.7	400	"	Nil	0

subjected to acute toxicity tests (intravenous and subcutaneous) and chemical analyses with regard to their antimony contents. For comparison, Bayer's 'neostibosan' (diethylamine salt of *p*-aminophenylstibinic acid) has also been tested side by side. As usual, the toxicity

tests were carried out on white mice (weight varying from 14 to 16 grammes). The results obtained are summarized in table III.

Discussion

The exact composition of urea stibamine has not as yet been settled, though the recent

studies of Gray *et al.* (1931) and of Datta *et al.* (1945) have thrown some light on the possible composition of the drug and the difficulties underlying this problem. A compound whose chemical identity is not established, or one whose relative constituents are not known, is naturally liable to show variation in its animal toxicity during preparation of different batches. For the preparation of a drug, all lots of which should conform to a fixed standard of toxicity, it is essential to ascertain the causes of variation in toxicity. Recently, it has been observed by Datta *et al.* (1945) that the complete removal of free uncombined urea from urea stibamine leads to an increase in its toxicity. Thus, the presence of some trace of urea seems to be necessary to reduce the toxicity of the drug within certain limits.

From the observations recorded in this paper, it is evident that, although the toxicity of urea stibamine somewhat increases with the increase in the total antimony content of the drug, still the latter is not the sole cause for the generation of toxicity. Sometimes a sample containing less antimony is found more toxic than one with a higher antimony content. Artificial reduction of antimony content of such a sample by the addition of anhydrous glucose does not bring down its toxicity within the normal limits. At the same time, it is found that urea stibamine containing 41 to 42 per cent antimony can be prepared in such a way as to pass the toxicity test in an intravenous dose of even 275 mg./kg. It is, therefore, evident that the toxicity of urea stibamine does not depend solely on the total antimony content but is influenced to a great extent by the presence of antimonious acid, as is shown by a scrutiny of the ratio of the percentage of antimony present as antimonious acid to that present in pentavalent organic combination (*vide* table II). It is observed that increase in this ratio above a certain limit (1 : 26) tends to bring about a definite increase in the toxicity of the drug.

It would be interesting to note here that Bose, Iyengar and Mukerji (1945) have found the LD₅₀ of urea stibamine to be 215 mg./kg. with a sample whose antimony content present as antimonious acid was found to be definitely high (2.7 per cent). All these observations suggest that, apart from the percentage of total antimony content, other factors (such as, the presence of antimonious acid) are responsible for the development of toxic reactions; and that, prepared carefully under certain standardized conditions, urea stibamine can be made to satisfy much higher standards of toxicity tests than those accepted at the present time (namely, 200 to 225 mg./kg. intravenously; compare Guha, Dutta and Mukerji, 1943).

In the case of the secondary and tertiary amine salts of *p*-aminophenylstibinic acid, it has been observed that unless specifically prepared, the derivatives are likely to give rise to more toxic reactions than expected. In order

to obtain these salts devoid of undue toxicity, these amines must be in a state of high purity, and should be absolutely free from any other complex amine*.

From an analysis of the data regarding the toxicity of urea stibamine and the diethylamine salt of *p*-aminophenylstibinic acid, it appears that though the percentages of antimony in these two compounds do not vary markedly, the variation in their relative toxicities is, however, very well marked. Considering that all these compounds are derived originally from *p*-aminophenylstibinic acid, this lowering of toxicity in the cases of diethylamine and tri-*iso*-propylamine salts appears to be a function of the nature of salt formation. Here, antimony acts as a secondary factor, allowing its toxic properties to be modified according to the virtue of the reaction base.

With regard to the diethylamine salt of *p*-aminophenylstibinic acid, some experimental evidence has been obtained which indicates that the toxicity of this salt can be further lowered by incorporating a minute trace of a suitable reducing agent. Further work on this point is in progress.

Summary

1. The toxicity of a large number of samples of urea stibamine and other pentavalent organic antimony derivatives has been studied in relation to their antimony contents.
2. It is found that the toxicity of urea stibamine does not depend solely upon the total antimony content but is influenced by the presence of antimonious acid.
3. It is found that urea stibamine, if carefully prepared, can be made to satisfy much higher toxicity limits than those accepted at the present time (namely, 200 to 225 mg./kg.).
4. The toxicity of the diethylamine and tri-*iso*-propylamine salts of *p*-aminophenylstibinic acid depends to a considerable extent on the purity of these amines used.

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* It has been previously observed in this laboratory by one of us (A. N. B.) during the preparation of tri-*iso*-propylamine salt of bismuth that, unless the amine is repeatedly distilled and used in a very pure state, the salt, though satisfying the chemical tests, gave rise to a severe type of gangrene of the limbs of the injected animals.

THE CAUSE OF HYPERGLYCÆMIA UNDER GENERAL ANÆSTHESIA*

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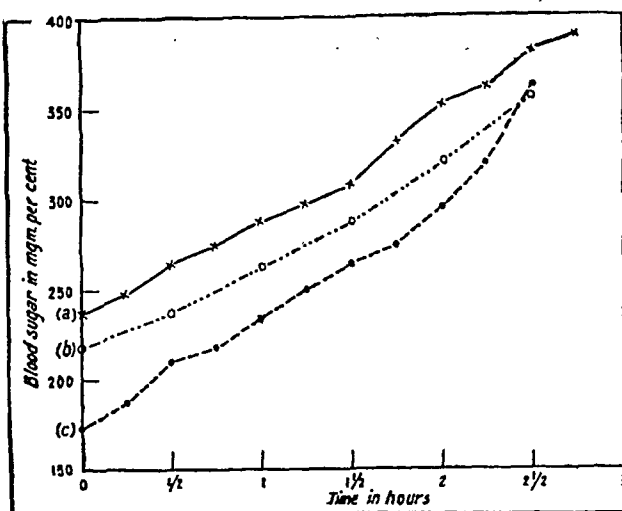
VARIOUS workers have studied blood-sugar levels during anæsthesia.

de Wesselow (1924) observed a definite rise of blood-sugar level in cases of prolonged inhalation of chloroform or ether, the cause of which was not determined. He stated that apparently it was not due to asphyxia, nor there was any evidence of its being pancreatic or adrenal origin. Swan (1911) and Atkinson and Ets (1922) who were earlier workers on this subject also found that ether produced some hyperglycæmia in normal animals. Lawrence (1929) stated that liver glycogen is mobilized during all forms of anæsthesia, and probably ether shows the most marked action of this nature. Mahler (1926) and Ross and Davis (1920) observed deficiency or direct depression of the internal secretion of the pancreas produced by ether anæsthesia in dogs and thought that this led to hyperglycæmia. Minnitt (1932) not only observed a rise of the blood-sugar level after ether anæsthesia, but also noted that the sugar tolerance was diminished by it. He also noted a post-operative diminished sugar tolerance in cases of local anæsthesia produced by novocain. He therefore suggested that the anæsthesia was not directly the cause of the inefficiency of the pancreas. He also found that ether produced a great rise in blood sugar, and in every case it was above 200 mg. per cent; it was much higher at the end of the operation than at the beginning; it then gradually came down. Pratt (1938) observed that ether has a direct stimulating effect on the production of adrenaline. He also stated that, in spite of statements to the contrary, cyclopropane is also capable of raising the blood sugar, though the effect is not so marked as that of ether. Minnitt in his discussion on Pratt's paper (Pratt, 1938) suggested that the rise of blood sugar varied with the depth of anæsthesia.

Some observers still believe that there are a few general anæsthetics which do not produce any rise in blood sugar, yet from all the data available it appears that every general anæsthetic produces at least some rise of blood-sugar level.

This investigation was undertaken to find out the cause of hyperglycæmia and also the relationship between the depth of anæsthesia and the amount of hyperglycæmia produced. In order to obtain steady and uniform results, urethane was selected for this investigation (unless otherwise stated), and cats were used in all these experiments. Two grammes of urethane per kilogram body weight of cats were given intramuscularly, and the estimations of blood-sugar level were started 3 hours after the administration of the urethane and continued for about two and a half hours. At that time all the animals did not show the same degree of anæsthesia. In some the anæsthesia was very light, whilst in others it was deep. The blood sugar was tested in blood taken from the femoral vein, with the

least possible operative interference, at intervals of 15 minutes, and the result, in some typical cases, has been recorded in graph 1. It will be noticed from this graph that, in those animals in which anæsthesia was light, the blood sugar at the beginning of the observation was much lower than that in animals in which anæsthesia was deep. Moreover, even in the lightly anæsthetized animals towards the end of the observations, with the increase in the depth of the anæsthesia, the blood sugar also rose. The blood-sugar level in all the cases at the end was more or less the same. The sugar curve presented a practically linear ascent, especially at the beginning of the observations, whereas, towards the end, the rise was more



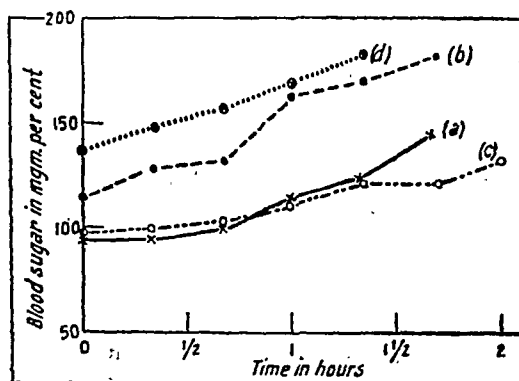
Graph 1.

Urethane anæsthesia.

First observation 3 hours after administration of urethane.

(a) and (b)—Deep anæsthesia.
(c)—Light anæsthesia.

sharp in some of the cases (*vide* graph 1). Further, with chloralose as an anæsthetic (which produces a much lighter anæsthesia), the rise of blood sugar was much less than that seen with urethane (*vide* graph 2). Moreover, in



Graph 2.

Chloralose anæsthesia.

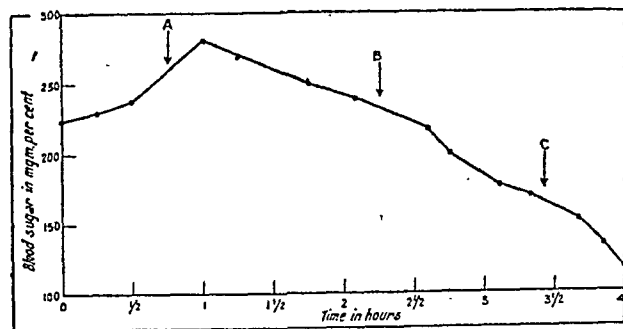
(a) and (b)—First observation 2 hours after chloralose.
(c)— " " 1 hr. 25 mts. "
(d)— " " 1 hr. 40 mts. "
(25 per cent more chloralose given.) "

*Read at the Physiology Section of the 33rd Session of the Indian Science Congress Association held in January 1946.

cat number (d) of this graph, which received 25 per cent more chloralose, the blood-sugar level was higher than that of the other cats which received the normal dose.

The effect of the depth of anaesthesia on the blood-sugar level was also studied in cats in which a dose of urethane just short of the anaesthetizing dose was given. In these animals, the depth of anaesthesia was suitably varied by further administration of ether. With the increased depth of anaesthesia, the blood-sugar level was increased, and, the deeper the anaesthesia, the greater was the rise in blood sugar.

Inami (1931) working on rabbits concluded that the degree of metabolic disturbance produced by ether narcosis depends on the tissue concentration of ether. If there is such a direct relationship between the tissue concentration of ether and the hyperglycaemia produced, then the hyperglycaemia would also be produced in spinal preparations by increasing the tissue concentration of the anaesthetic, which will inhibit the activity of the islets of Langerhans. Spinal cats were, therefore, prepared under urethane or chloroform and ether anaesthesia. The level of blood sugar was the highest immediately after the operation, but it immediately began to fall steadily. In these preparations further intramuscular injections of 10 to 20 per cent of the normal anaesthetic dose of urethane produced no further rise in blood sugar, but accelerated the fall (*vide* graph 3). This proved that the peripheral



Graph 3.

Spinal preparation under urethane with further doses of urethane.

- A.—Period of operation for spinal preparation.
- B.—10 per cent more urethane injected.
- C.—Another 10 per cent more urethane injected.

nervous mechanism took no part in the production of hyperglycaemia seen during anaesthesia, but it probably depressed the metabolic activity and produced a rapid fall in blood sugar. In these experiments the concentration of urethane was also certainly increased in the pancreas, but this increase in concentration, for some unknown reason, did not produce any rise of blood-sugar level. It, therefore, seems that the cause of hyperglycaemia under general anaesthesia must be sought in some factor not directly concerned with the pancreas.

This finding, that the peripheral nervous mechanism in spinal animals takes no part in the production of hyperglycaemia under anaesthetics, gave a very strong indication that the cause of hyperglycaemia during general anaesthesia must be sought in some part of the higher centres.

Fulton and Ingraham (1929) observed that tracts of fibres arise from the frontal lobe and pass to the centres in the hypothalamus; that division of these cortico-hypothalamic tracts releases the hypothalamus from the cortical control and hence produces a condition of chronic 'rage' in animals; there was also evidence of diffuse discharge of the sympathetic nervous system. They also showed that lesions in the pre-chiasmatic region of the hypothalamus produced increased 'wildness' in the animals. Bard (1928) demonstrated that decerebration posterior to the level used by Fulton and Ingraham produced the opposite effect, the animals which were 'wild' became docile. He, therefore, suggested that these subconscious manifestations were probably due to the activity of the posterior hypothalamic nuclei. During recent years it has been proved beyond doubt that the posterior hypothalamic region contains the sympathetic centre (Beattie and Sheehan, 1934; De, 1946) and stimulation of the posterior hypothalamic nuclei produces a condition of hyperglycaemia through the sympathetico-adrenaline mechanism (Houssay and Molinelli, 1925; Karplus and Kreidl, 1927; Beattie *et al.*, 1930).

From these experiments it is surmised that the general anaesthetics produce hyperglycaemia by releasing the hypothalamic sympathetic centre from the control of the cerebral cortex.

Discussion.—It has been shown that in the production of hyperglycaemia the pancreas does not take any direct part. Experiments have also been cited to show that the blood sugar varies with the depth of anaesthesia. The deeper the anaesthesia the greater has been the rise of blood sugar and *vice versa*. Beattie and Sheehan (1934) stated that chloralose causes the least depression of the central nervous system. A correspondingly reduced effect on the blood sugar has been obtained in my experiments with chloralose, as shown in graph 2. The blood sugar in these cases was about 100 mg. per cent at the beginning and even toward the end of the experiments the rise was very small compared to the rise of the blood sugar noted with anaesthetics like ether, urethane, etc., which produce a great depression of the central nervous system.

The already quoted experiments of Fulton and Ingraham (1929) show that the cerebral cortex under normal circumstances exerts an inhibitory influence over the hypothalamic sympathetic centre. Under the condition of anaesthesia, this inhibitory influence is removed to a greater or less extent. In lighter anaesthesia, the cortical inhibition is removed to a less extent, and therefore the rise in blood sugar is smaller, whereas with the deepening of the anaesthesia, as more and more of the cortical control was withdrawn, the greater was the rise of blood-sugar level. From all the foregoing facts it is reasonable to conclude that the production of hyperglycaemia under general anaesthetics must be due to inhibition of the cortical

control, which is normally exercised over the hypothalamic sympathetic nuclei.

Summary

(1) The blood sugar under general anaesthesia varies directly with the depth of anaesthesia.

(2) The peripheral nervous mechanism takes no part in the rise of blood sugar under anaesthesia.

(3) The hyperglycaemic effect is due to release of the hypothalamic sympathetic centre from the normal cortical control.

In conclusion I express most sincere thanks to Lieut.-Colonel R. Linton, B.Sc., M.B., Ch.B., I.M.S., Principal, Medical College, Calcutta, for kindly affording all facilities in carrying out this investigation. I also thank my assistants for their ungrudging help in connection with this work.

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NOVOCAINE INFILTRATION IN ACUTE SPRAINS

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SPRAIN is a very common traumatic injury, but there is no unanimity of opinion as to the actual nature of the lesion and the structures involved in it. In actual practice, a variety of traumatic conditions in the neighbourhood of joints presenting the typical signs and symptoms, but which reveal no fracture or dislocation, are labelled as sprains; cases involving different peri-articular and articular structures are also included.

Theoretically sprain is considered to be a stretch and partial rupture of ligaments, tendons, or muscles, in, around and near a joint,

producing the typical syndrome*. There are two views as to the mechanism of production of the syndrome, namely, the reflex theory, and the mechanical theory. According to the mechanical theory it is believed that although the ligament is not torn right through, its various fibres and fasciculi do snap across, and that the syndrome is due to the resulting reparative inflammation; and that therefore it should be treated by strapping or support of the part in a plaster cast. This will bring the severed ends of fibres in close approximation and keep them at rest while healing takes place. Leriche and others believe in the reflex theory. They think that there is no macroscopical tear in the ligament and that the syndrome is due to overstimulation of the nerves and sense organs so richly supplied in and around the joints. At the time of injury, these nerves and sense organs get over-excited and upset the vasomotor equilibrium of the part, causing effusion. The effusion of fluid liberates substances, which further irritate the nerve endings and thus give rise to the sprain syndrome. Leriche exposed cases of sprain at operation and failed to find any bruise or tear in ligaments. He tried local novocaine infiltration in the treatment of sprains and obtained good results. He attributes its efficacy to blocking of afferent impulses. His findings were corroborated by others. The writer tried Leriche's method of novocaine infiltration in 50 cases of acute sprain, and this report embodies his observations on these cases.

Method.—After careful examination to exclude fracture, dislocation and complete tear of ligaments, cases were provisionally diagnosed as sprain. The diagnosis was verified by further examination after infiltration of novocaine, when the part became insensitive and the muscular spasm was abolished. No radiological examination was done. Two per cent novocaine solution was used, and no adrenalin was added to it. The infiltration of peri-articular structures was done widely and liberally. The patients were encouraged to move the joints actively after infiltration.

Observations.—Relief of pain was immediate. Almost full range of movement was possible soon after the injection. Eleven out of the 50 cases reported, on questioning, reappearance of the pain on the first night, generally 7 to 10 hours after the infiltration. It was not severe enough to call for medical attention, though in some cases sufficient to disturb sleep. It lasted 3 to 5 hours and disappeared spontaneously. The swelling and tenderness disappeared completely in 24 to 72 hours, and full mobility, unattended by pain, was restored. Most of the patients were cured on the third day and declared fit for duty next day. No complaint was

* Some define the stretch and partial tear of muscular and tendinous fibres as a separate condition and term it as 'strain', in contradistinction to 'sprain' which indicates the lesion of ligaments only.

made by the patients of 'after pain', a distressing symptom reported by Moynahan (1939).

The parts affected were as follows:—

Name of the joint	Number of cases
Ankle	34
Finger	5
Wrist	4
Big toe	4
Knee	2
Thumb	1
TOTAL ..	50

The duration of injury before treatment was as below:—

	Number of cases
Less than 12 hours	4
12 to 24 hours	18
1 to 2 days	23
2 to 3 days	3
3 to 4 days	2
TOTAL ..	50

No correlation, either positive or negative, was observed between the duration of injury before treatment and the time taken for complete cure.

The cases were classed as severe, moderate and mild according to the degree of severity of symptoms.

	Number of cases
Mild	16
Moderate	26
Severe	8
TOTAL ..	50

Mild cases were almost cured within 24 hours. Moderate and severe cases took 2 to 3 days for complete recovery. In mild cases no complaint of 'after pain' was elicited on questioning.

The period of incapacity after commencement of treatment in 34 cases of ankle sprain was as below:—

Period of incapacity	Number of cases
1 day	3
2 days	8
3 days	23
TOTAL ..	34

On computation, the average period of incapacity in cases of ankle sprain treated with novocaine comes to 2.6 days and agrees with that of Moynahan. The shortened period of incapacity stands in sharp contrast with the period of incapacity of 10 to 15 days in similar cases treated otherwise. The figures quoted by Moynahan in connection with cases of ankle

sprain treated with and without novocaine are given below:—

	Number of cases	Average period of incapacity
<i>Ankle sprain treated without novocaine</i>		
Dundee Royal Infirmary, 1936	41	12.1 days
Royal Air Force, Tangmere, 1937-38.	12	10.2 days
<i>Treated with novocaine</i>		
Dundee Royal Infirmary, 1937	17	2.8 days
Royal Air Force, Tangmere, 1937-38.	17	2.1 days

Follow-up findings.—Most of the patients treated in the present series were police constables; hence it was possible to follow them up for 2 to 3 months. In none was any limitation of movement of the joint discernible, or any weakness of the joint.

The end results were uniformly good.

Summary and conclusions

Fifty cases of acute sprain involving various joints treated with local infiltration of novocaine solution are reported. The end results were uniformly good. The average period of incapacity in 34 cases of ankle sprain in this series was 2.6 days.

The strikingly shortened period of incapacity with novocaine treatment is a great advantage. The immediate abolition of pain, the restoration of almost full mobility soon after injection, the uniformly good end results, and the simple and ambulatory nature of this treatment make it widely applicable.

Acknowledgment

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A NOTE ON PHLYCTENULAR OPHTHALMIA IN ADULTS

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THE view is widely held that phlyctenular keratoconjunctivitis is a disease of childhood and early adolescence, and that it is rare in adults (Duke-Elder, 1938; Parsons, 1942; Sorsby, 1942). There is a tendency to consider all cases occurring in adults as being pseudo-phlyctenulosis of the tropics (Sorsby, 1942). Clinically, however, such cases are indistinguishable from those seen in children and in adolescents.

The incidence of the disease in adults has been reported by many workers in the East. The

following facts are taken from the published records (Sorsby, 1942):—

In Japan, Kuboki (1924) is of the opinion that infection occurs predominantly in adults, a view also shared by Attiah (1935) in Egypt, and Boen Lian (1930) in Dutch East Indies. According to Wang (1934) in Shanghai the disease is very common in adults, but is quite frequent in children too.

Diagnosis.—In simple phlyctenular conjunctivitis in adults the diagnosis does not present any difficulty. The situation of a raised pinkish nodule in a hyperæmic area, at or near the limbus, is so typical as hardly to be confused with any other condition. Three conditions may, however, have to be distinguished in some cases (Duke-Elder, 1938):—

(i) Episcleritis, (ii) acne rosacea, and (iii) vernal catarrh (limbal type).

In episcleritis, phlycten-like nodules never appear, and moreover the swelling and congestion are deeply situated and the epithelium never breaks. Acne rosacea on the cornea or conjunctiva is invariably associated with similar lesions on the face. The clinical picture of spring catarrh is quite distinct. The typical gelatinous hypertrophy of the conjunctiva with no phlyctenular nodules, the absence of itching or seasonal recurrence, and the presence of eosinophils in conjunctival smears are the salient points in differential diagnosis. In cases of keratitis attention has to be paid, in infective types, to the demarcating margin. Such ulcers may be associated with hypopyon or iritis, and pannus of course is absent.

Personal observations

Age incidence.—A series of 484 cases of phlyctenular keratoconjunctivitis were examined in the eye out-patient department of the Mayo Hospital, Lahore. An investigation into these cases has been reported (Sayed and Shah, 1945). Out of these 484 cases, 138 (28.9 per cent) were in those over the age of 20 years. The percentages of cases in children and adults recorded by different authorities are given in

TABLE I
Phlyctenular ophthalmia in children and adults

Author	Total number	PERCENTAGE OF TOTAL NUMBER	
		Children, 0-19	Adults, 20-60
Guttman (1898) ..	6,550	87.4	12.4
Krasso (1925) ..	1,283	61.3	31.1
Gronholm (1926) ..	1,500	88.0	10.0
Weekers (1929) ..	1,394	84.1	15.0
Rolet (1931) ..	2,495	81.0	18.9
Essen-Moller (1936)	2,614	81.4	18.5
Frominopoulos (1940)	2,970	63.0	36.1
Sayed and Shah (1945)	484	71.3	28.9

table I (modified from Sorsby, 1942), and compared with those in the present series. This confirms, to some extent, the view expressed by Herbert (1898) that in India one-third of all cases of phlyctenulosis occur in those over the age of 20 years. Analysis of the table reveals the interesting fact, not generally recognized, that the incidence of the disease in adults, even in the West, is not negligible.

In table II are given the percentages of total number (children and adults) in various age

TABLE II
Distribution by age groups

Author	PERCENTAGE OF TOTAL NUMBER IN VARIOUS AGE GROUPS				
	20-24	25-29	30-49	50-59	Over 60
Guttman (1898) ..	5.2	7.2	..
Krasso (1925) ..	12.8	7.0	9.2	1.5	0.6
Gronholm (1926) ..	9.0	1.0
Weekers (1929) ..	8.0	2.3	5.7
Rolet (1931) ..	8.7	5.0	4.7	0.5	..
Essen-Moller (1936)	8.8	3.7	5.1	0.7	0.2
Frominopoulos (1940)	10.0	7.7	13.7	3.4	1.3
Present author (1945)	15.2	3.7	8.6	0.8	..

groups by different authorities, compared with those in the present series. It will be seen that there is general agreement among the various authors that the maximum number of cases in adults occur in the age group 20 to 24 years.

Sex incidence.—In patients below the age of 20, the girls and boys have been reported to form 60.9 per cent and 39.9 per cent respectively (Sorsby, 1942). This finding has not been confirmed in the case of Indian patients, in whom the figure is given as 51.6 per cent in boys and 48.3 per cent in girls (Sayed and Shah, 1945). The slightly higher figures in the children become more pronounced in adults (table III).

TABLE III
Percentage distribution of cases by sex and age

Age group	Author	Male	Female
Children, 0-19.	Sorsby (1942) ..	39.1	60.9
	Sayed and Shah (1945)	51.6	48.3
Adults, 20-60.	Wang (1934) ..	64.4	35.6
	Present author (1946)	66.6	33.3

It has been stated by Wang (1934) that in Shanghai males comprised 64.4 per cent and the females 35.6 per cent of the total number of cases seen in adults. He suggested that the difference might be artificial, as the Chinese women do not seek medical advice readily. In the present series males comprised 66.6 per cent and females 33.3 per cent of the total number of adult cases, thus confirming Wang's findings.

As, however, there is no evidence that the Indian women are slow in seeking medical advice, the difference between the incidence of the disease in the two sexes would appear to be real rather than artificial.

Apart from the above variations in the age and sex distribution there does not appear to be any other significant difference in the clinical occurrence of the disease in children and adults. There is no difference in the seasonal and community distribution of the disease; and the position of the phlyctens, the incidence of keratitis, of superadded infection, of cervical lymphadenitis and nasopharyngeal sepsis, is about the same in adults as in children.

Summary

The clinical occurrence of phlyctenular keratoconjunctivitis in adults is discussed. It is concluded from an investigation into a series of 138 adult cases, that apart from the variations in the age and sex incidence the disease, clinically at least, differs in no significant way from that in children.

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THE 'BURNING-FEET' SYNDROME

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THE deficiency disease described in this paper under the not very satisfactory title of 'burning feet' has certain well-marked and constant clinical features and is a definite clinical entity. It appears to be common among the poor in South India—decidedly more common than 'peripheral neuritis' associated with thiamine deficiency.

Outbreaks of 'burning feet' have previously been reported among malnourished populations and have often occurred in jails. The disease has not, however, hitherto been adequately observed and described and has often been confused with peripheral neuritis. The differences between 'burning feet' and the peripheral neuritis associated with thiamine deficiency, are, however, so fundamental that it is surprising that the two conditions have been confused.

Incidence

The disease is met with in people belonging to the poorer class. Only 8 cases in the series of 53 cases investigated had monthly incomes per family of over Rs. 50. Forty-one patients were living on monthly incomes ranging between Rs. 20 and Rs. 30 per family, while in four cases the monthly family income was below Rs. 20. All the patients were rice-eaters, mostly living on rice gruel and cheap vegetables; the rice consumed was in most cases of the parboiled type—a significant fact since the latter contains enough thiamine to prevent beri-beri. Females were more commonly affected than males; the present series included 39 females and 14 males. The common age incidence was between 20 and 40 years; 44 patients were between these age groups, 6 were below 20 and 3 above 40 years. A history of delivery, a few weeks prior to the development of the symptoms, was given by 27 of the 39 female patients of the series.

Clinical observations

The patients showed obvious evidence of malnutrition. Signs suggestive of riboflavin deficiency were almost invariably present. The tongue was clean, large and pinkish; showing at its edges multiple short transverse fissures while the centre was traversed by a few longitudinal fissures and bordering these fissures were prominent hypertrophied flat-topped papillae. Inflammation of the angles of the mouth was present in a majority of cases. Angular blepharitis and evidence of superficial keratitis were encountered in several patients. Eczematoid dermatitis of the scrotum was observed in a fair number of the male subjects, while leucorrhœa was common in a large number of the female patients. Only 5 of the 53 cases reported on here did not show signs suggestive of ariboflavinosis, and even in three of these cases a history of soreness of the tongue at some previous date was obtained.

A burning sensation in the extremities is the characteristic feature of these cases, and it is to obtain relief from this that the patient comes to the hospital. The burning sensation is usually confined to the soles of the feet, but is present in some cases, in the palms of the hands as well, patients describe their complaint by the Tamil words 'Kal erichal' which literally mean burning of the feet. No cases in which the hands alone were the sites of burning sensation have been met with. Characteristically, the sensation of burning starts in the soles of the feet round about the ball of the great toe and seems to spread therefrom to involve the soles completely. In some cases, the burning sensation may spread upwards to involve the dorsum of the feet and the ankle region. The burning may be quite mild and tolerable, but is frequently most intense and incapacitating. It may come on in paroxysms, the patient having excruciating agony for a short period

and then remaining free from the symptom for the rest of the day. Some patients seem to obtain relief by wrapping their feet in a wet cloth. Others find the contact of their feet with cold or hot objects intolerable and prefer to leave their feet alone.

The patient also complains of a feeling of 'pins and needles' in the distal parts of the extremities. This is distinct from the burning sensation referred to above. It is mostly felt on the dorsum of the feet and round about the ankles. Varying grades of intensity of 'pins and needles' are met with. In some cases it may be so mild that the patient refers to it only on being questioned; in others it may be so severe as to cause restlessness and sleeplessness. There is no invariable parallelism between the burning sensation and the feeling of 'pins and needles'; both may be present in severe degrees in the same patient, or one may be intense and the other mild. Both these subjective sensations get worse while the patient is walking about. The feet feel sore when brought into contact with hard ground, and consequently the patient may be bed-ridden most of the time.

In striking contrast to the marked subjective symptoms is the paucity of objective signs, even in cases which have had the disease for over 2 years. The limbs do not show any wasting. Foot-drop, so commonly seen in advanced and neglected cases of peripheral neuritis, is never observed in these cases. The limbs are not spastic and their muscular power is not diminished. The knee jerks are brisk, the abdominal reflexes are preserved and the plantar response is flexor. There is no loss of sensation of any kind; touch, temperature and pain sensations, the vibration sense, the sense of position and passive movement are all retained even in advanced cases. A striking feature is the absence of tenderness in the calf muscles. Indeed, the patient may find slight temporary relief from the distressing symptoms when the calf muscles are squeezed. Unsteadiness of gait is met with in some advanced cases, but is evidently due to the discomfort caused by the contact of the feet on the hard ground and does not signify loss of the sense of position.

An interesting feature observed in several cases is hyperidrosis of the affected parts. Visible beads of perspiration may stand out, and the feet may be moist to the touch. The hyperidrosis is sharply delimited to the parts where the burning sensation is felt, namely, the feet, and in a few cases the palms of the hands as well. Abnormal perspiration over other parts of the body is not seen. In cases where the paræsthetic symptoms come on in paroxysms, the hyperidrosis sets in a short while after the burning sensation has started and continues for a short while after the burning sensation has disappeared.

Treatment

The response of the cases to intensive treatment with vegemite (marmite substitute) was first studied. Thirteen cases were treated with 4 to 6 drachms (15 to 22½ grams) of vegemite twice daily for periods ranging from 3 to 4 weeks. Definite improvement was obtained in all the 13 cases; the burning sensation and the feeling of 'pins and needles' subsided, and by the end of the fourth week of treatment the subjective symptoms had completely disappeared in all cases.

The next step was to attempt to discover the factor in marmite responsible for the curative effect. Thiamine in a 50 mg. dose daily by injection was tried on a group of 10 cases for a period of about three weeks. No improvement was obtained in any of these cases. Nicotinic acid (300 mg. daily by the oral route in 4 cases and 100 mg. daily by the parenteral route in 4 other cases), given over a period of about three weeks, was equally ineffective in inducing improvement. A group of 12 cases was treated with 10 mg. of riboflavin daily by mouth for periods ranging from 2 to 3 weeks. With this treatment there was rapid subsidence of the associated signs—glossitis, angular stomatitis, ocular symptoms, etc., but the burning sensation continued with unabated severity; indeed a few patients reported that this was worse at the end of treatment.

The response to treatment with pantothenic acid was investigated. The cases were treated for periods ranging from 2 to 3 weeks with 20 to 40 mg. of calcium pantothenate injected intramuscularly daily. Definite improvement was obtained in all the ten cases. The improvement was more striking and rapid than that obtained with vegemite; indeed in cases where 40 mg. of the drug daily were employed, the patient reported improvement within the 5th day of treatment, and the improvement was complete by the end of a fortnight of treatment. The burning sensation was the first symptom to disappear under the treatment. With the disappearance of the burning sensation, the hyperidrosis of the affected parts also ceased. The feeling of 'pins and needles' persisted for a few days after the 'burning' had stopped, and was the last symptom to disappear.

The patients tolerated injections of calcium pantothenate well; no untoward reactions were noticed when even 80 mg. of calcium pantothenate were administered in a single dose by injection. It would seem that 40 mg. daily by injection is a suitable dose for a case of moderate severity; the very severe case, in which the burning sensation is continuous and excessive, may need as much as twice this dose daily. A fortnight appears to be about the duration of treatment necessary to control the symptoms in mild cases, while in severe cases the treatment may have to be continued for about a week longer.

TABLE I
Response to treatment

Group	Number of cases*		Drug employed	Dosage	Duration	Response
	Out-patient	In-patient				
1	7	6	Vegemite	4 drams twice daily	3 to 4 weeks.	Complete subsidence of symptoms in 4 weeks.
2	6	4	Thiamine	50 mg.	About 3 weeks.	No improvement.
3	5	3	Nicotinic acid.	(4 cases) 300 mg. orally or 100 mg. I.M.	About 3 weeks.	No improvement.
4	7	5	Riboflavin	10 mg. orally	2 to 3 weeks.	No improvement in 'neuropathic' signs.
5	3	7	Calcium pantothenate.	20 to 40 mg. I.M.	2 to 3 weeks.	Complete improvement in 3 weeks.

*To exclude the possibility of the hospital diet vitiating the results, a number of cases in each group were treated as out-patients and thus were allowed to subsist on their usual, normal diet during the period of treatment.

Discussion

The incidence of the disease among very poor people, the presence of associated signs of riboflavin deficiency and the improvement of the burning sensation by means of the administration of marmite indicate that this disorder is a food deficiency disease. The uniform improvement in all cases on treatment with marmite shows that the deficient factor is present in marmite. Since intensive treatment with thiamine, riboflavin and niacin were ineffective, the deficient factor is evidently something different from any of these. The striking improvement obtained with calcium pantothenate suggests that the disorder is probably the result of deficiency of pantothenic acid in the diet and that the improvement obtained with marmite is due to its pantothenic acid content.

In Spain, Peraita (1942), working among the victims of the famine precipitated by the civil war, described several varieties of neurological manifestations in malnourished subjects. The 'paræsthetic-causalgie syndrome' reported on by Peraita would seem to resemble the syndrome here described. Peraita obtained good results in his cases with yeast but found thiamine, niacin and riboflavin ineffective, and concluded that some factor in the vitamin B₂ complex other than niacin and riboflavin was responsible for the curative effect of yeast.

The very close and invariable association of established signs of ariboflavinosis in these cases is a significant finding. Stannus (1944) has, indeed, suggested that 'burning feet' is part of the syndrome of ariboflavinosis. It has, however, been found that riboflavin was ineffective in relieving the symptoms, and this observation is in accord with Peraita's finding in Spain. The explanation for the close association of signs of riboflavin deficiency with signs of pantothenic acid deficiency may lie in the

fact that the functions of these two vitamins in human nutrition are closely interrelated, and possibly in a similarity of their distribution in food. The observation of Spies and his associates (1940) that the injection of pantothenic acid causes a rise in the blood level not only of pantothenic acid but also of riboflavin, and similarly that the injection of riboflavin causes a rise in the blood level not only of riboflavin but also of pantothenic acid, is interesting proof of the close interrelationship of the two vitamins. For this reason a combination of riboflavin and pantothenic acid is likely to yield better results than pantothenic acid alone in these cases. Indeed, the quantity of pantothenic acid supplied through vegemite did not probably far exceed 15 mg. daily—a quantity much less than that apparently needed when pantothenic acid was given alone. But the good results that were, nevertheless, obtained with vegemite therapy probably resulted from the mutual potentiation of action of the closely interrelated vitamins of the B₂ complex.

The question of the nature and the site of the lesions responsible for the 'nervous' symptoms is one of considerable interest. The differences between the syndrome here described and peripheral neuritis associated with thiamine deficiency have been already pointed out, and are indicated below for purposes of clarity.

TABLE II

Burning feet	Peripheral neuritis
1. No impairment or loss of sensation.	Varying degrees of impairment of sensation present.
2. Knee jerks brisk	Knee jerks diminished or absent.
3. No loss of muscle power.	Loss of muscle power present.
4. No tenderness of the calf muscles.	Tenderness of the calf muscles present.
5. No muscular wasting or foot-drop present.	Muscular wasting and foot-drop present.

It is true that in very early cases of peripheral neuritis, the objective signs mentioned above may be absent. It must be pointed out, however, that many of the cases of burning feet here observed had had the disease for over 2 years when they were first seen and could scarcely be called early cases. Moreover, tenderness of the calf muscles, a diagnostic sign of peripheral neuritis even in the early stages, was invariably absent in these cases. Beri-beri, which is definitely known to be related to thiamine deficiency, is very rare in this part of the country, presumably because the bulk of the poor population subsist on par-boiled rice. In the Northern Circars, on the other hand, where raw rice takes the place of par-boiled rice as the staple cereal, beri-beri is common, and peripheral neuritis associated with tender calf muscles, foot-drop and wasting is correspondingly much more in evidence there than in Madras (Iswariah and Kutumbiah, 1934). A diagnosis of peripheral neuritis in the cases of 'burning feet' described here is thus unwarranted, both on clinical grounds and on the basis of prevailing local dietetic habits. Lesions of the peripheral nerves of some duration must cause sensory and motor changes; in the absence of these, one must look elsewhere for the lesion.

Discussing the probable pathology of 'burning feet' in ariboflavinosis, Stannus (1944) suggests that the site of the lesion may be in the thalamus; lesions of the lateral nucleus of the thalamus are known to produce the 'thalamic syndrome' of Dejerine and Roussy, characterized by intense paræsthetic sensations. A lesion of the thalamus that would cause subjective paræsthetic sensations without interfering with the appreciation of sensation must be strictly localized to the lateral part of the thalamus. Apart from other objections to Stannus' hypothesis, it is difficult to conceive of such a strictly localized lesion in the central nervous system resulting from dietetic deficiency.

It is possible that the burning sensation may be due to abnormal and excessive stimulation of the peripheral sensory nerve endings by certain intermediate metabolites accumulating in the tissues as a result of disturbance in cellular metabolism caused by the vitamin deficiency. Or, as Lewis has suggested with regard to the condition which he designates as erythralgia, there may be a release into the skin under such circumstances of some substance which lowers the threshold of certain sensory nerve endings. The presence of marked subjective symptoms in the absence of impairment of sensation and motor power is in accord with this suggestion.

On the other hand, the burning-feet syndrome bears some resemblance to the vasomotor disorders, acroparæsthesia and erythromelalgia; dysæsthesia and hyperidrosis are common to both of these. This would suggest that the burning-feet syndrome is primarily a vasomotor disorder caused by a central or peri-

pheral lesion. If the syndrome is a vasomotor disorder due to a peripheral lesion, the question has to be decided whether the vasomotor disturbance is the result of vasoconstrictor paralysis caused by the degeneration of fine nerve branches, as Weir-Mitchell suggested in the case of erythromelalgia, or the result of vasodilatation induced by the liberation of histaminoid substances in the tissues as suggested by Lewis.

Wintrobe *et al.* (1940, 1942) found that deficiency of pantothenic acid may be responsible for sensory neurone degeneration in pigs, and suggested that these findings might be applicable to man. Phillips and Engel (1939) on the other hand reported lesions in the spinal cord of animals fed on diets deficient in pantothenic acid, and suggested that pantothenic acid was necessary to keep the normal structure of the spinal cord intact. Lesions in the spinal cord must be expected to produce motor and sensory changes in addition to the paræsthetic symptoms; it is possible, however, that if the lesions are punctate and scattered, of the type reported by Phillips *et al.*, the considerable overlapping in the territories of distribution of the nerve fibres may mask the sensory and motor changes and the paræsthesia alone may be evident. A definite pronouncement on the nature of the lesion must, however, await a careful and detailed post-mortem examination of the nervous system in typical cases.

Summary and conclusions

1. A group of 53 cases of 'burning feet' has been investigated. The condition was found in close association with signs of ariboflavinosis.
2. The symptoms were relieved by marmite therapy, and by injections of calcium pantothenate, but were not influenced by treatment with thiamine, nicotinic acid and riboflavin.
3. The differences between the syndrome and peripheral neuritis are discussed, and the probable nature and site of the lesion in cases of 'burning feet' is discussed.

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[Note.—From personal experience the editor can record the very common occurrence of 'burning feet' in Hyderabad, Deccan, where years ago he saw many such cases for which there was then no explanation and no treatment.—Editor, I.M.G.]

A CASE OF LUMBO-SACRAL INTER-VERTEBRAL DISC HERNIATION CAUSING 'SCIATICA'

By G. P. CHARLEWOOD, M.B., Ch.B., M.R.C.O.G.

Civil Surgeon, Ajmer-Merwara, Ajmer

CONSIDERABLE argument has taken place in recent years in the medical press as to the frequency of herniation of the nucleus pulposus of the lumbar intervertebral discs as a cause of pain along the course of the sciatic nerve. Some authorities such as Dandy believe that with few exceptions sciatic pain is always due to such a ruptured intervertebral disc. Most others would be unwilling to go as far as this, but nevertheless it is becoming increasingly clear from the voluminous literature on the subject that herniation of the nucleus pulposus is a common cause of sciatic pain and must be seriously considered in every persistent case. It is worth remembering too that, in more severe lesions, hyperæsthesia in the 'saddle' area may develop, bladder function may become impaired, and paresis of one or both legs may occur. In about half the cases a history of injury may be elicited.

Case history

The patient, a policeman, aged 30 years, started getting pain along the course of the sciatic nerve some eight months previously. It was of a fairly severe nature making it impossible to carry on his duties as a policeman or even to walk about without pain. There was a history of an injury two years previously when he fell from a bicycle and injured his ankle. He did not remember any injury to his spine at the same time. Various types of treatment had been given to the patient for sciatica, such as massage, diathermy, manipulation of the sacro-iliac joint, injections of saline or novocaine into the nerve or its surroundings, etc. None was successful.

On examination, there was wasting of the gluteal and thigh muscles, and tenderness along the course of the sciatic nerve. There were no abnormal neurological signs. The patient seemed genuinely keen to get well and back on duty as he was afraid of being passed over for promotion, so it was considered that the presence of a psychological basis of the symptoms could be excluded. Further investigations were therefore undertaken to try to establish the nature of the lesion. A plain x-ray photograph of the lumbar vertebra showed nothing except a narrowing of the lumbo-sacral intervertebral disc which is thought to be of some diagnostic significance in herniation of the disc material. A lumbar puncture showed no abnormality, and the Queckenstedt test showed no spinal block. 30 c.cm. of air were injected into the spinal canal and

an x-ray plate (air myelograph) of the lumbar region was taken, but no definite evidence of any disc protrusion was found.

In spite of these negative findings the persistence of pain and the keenness of the patient to have something done seemed to warrant an exploratory laminectomy. This was done in the usual way, the anterior wall of the canal being visualized by retracting the unopened dura mater to the left. A definite herniation of the disc material, about the size of a pea, was seen at the lumbo-sacral joint, and was removed easily by blunt dissection.

On coming round from the anæsthetic, the patient stated that his old pain had completely gone, and though he had some unexplained tenderness in the calf muscles, this steadily decreased and was gone within a fortnight of his operation.

The only justification for publishing a single case of disc herniation is to help draw attention to what is undoubtedly a common but insufficiently recognized lesion.

My thanks are due to Rai Bahadur Suraj Narain for his co-operation.

A CASE OF CEREBELLAR APOPLEXY*

By KABIR HOSSAIN, M.B., D.T.M.

Professor of Medical Jurisprudence, Medical College, Calcutta

THE body of a woman aged 35 years was received for post-mortem examination under the following circumstances. The woman went out for marketing at 9 a.m. on 19th October, 1942, and was found unconscious on a rickshaw an hour later. She was removed to the Mayo Hospital where she died at 3-40 p.m. It was ascertained that she had been suffering from venereal diseases for the last ten days and had been given injections. The immediate cause of death as per the medical certificate was 'suspected opium poisoning'.

Post-mortem findings.—The body was fairly well nourished. Rigor mortis present all over the body; pupils dilated and equal; cyanosis present in finger nails. Internal examination—brain (2 lb. 10 oz.), effused clotted blood in the substance of the cerebellum; larynx and trachea contained froth; lungs congested and cedematous; heart (8 oz.), both sides contained fluid blood and post-mortem clots; stomach (6 oz.) congested with rugæ unduly prominent and containing 4 oz. brownish fluid; liver (2 lb.) slightly congested; gall-bladder contained thin bile; kidneys (3 oz. each) slightly congested; vulvæ ulcerated; uterus (3 inches × 2 inches × 1 inch) contained menstrual blood.

The chemical examiner's report revealed the presence of opium in the stomach and its contents, as well as in the liver and the kidneys.

Discussion.—Death in this case appears to be due to cerebellar apoplexy and not due to opium poisoning for the following reasons: (1) The characteristic signs of fatal opium poisoning such as marked cyanosis and venous congestion of the face approaching to blackness, extending down in front, the blue post-mortem staining, froth at

* Paper rearranged by the editor.

the mouth and nostrils and marked congestion of all internal organs were not noticed. (2) Though occasionally, in a fatal case of opium poisoning, hæmorrhages may be found in the pericardial cavity or in the skin on the face and trunk, and even congestion of the brain and its meninges, no cerebellar hæmorrhage has been noticed by me, nor is recorded in the literature. The presence of effused clotted blood in the cerebellar substance is therefore definite. (3) In opium poisoning, the symptoms advance gradually and the usual fatal period is 8 to 12 hours, the shortest on record being 45 minutes and the longest 2 to 3 days; in some cases ultimate recovery may also take place. In cerebellar hæmorrhage, as in this case, the onset of coma is sudden and abrupt and the great majority of the cases turn fatal; a case of hæmorrhage from the posterior inferior cerebellar artery extending into the cerebellum never survives; death rarely occurs within 2 hours.

Cerebellar apoplexy is not a very common condition. In our series of 1,608 autopsies done at the Calcutta Police Morgue during the three years from 1942 to 1944, only 25 cases were diagnosed as those of apoplexy, out of which 17 were due to cerebral hæmorrhage, 6 due to cerebellar hæmorrhage including the present one, and two due to pontine hæmorrhage. Cerebellar hæmorrhage occurs generally at earlier ages than cerebral hæmorrhage.

PENICILLIN IN THE TREATMENT OF AGRANULOCYTOSIS

By W. TREIBMANN, M.D.

C. I. Camp Hospital, Premnagar

IN the editorial of the May 1945 issue of the *Indian Medical Gazette*, penicillin has been suggested as the drug of choice besides pentose nucleotide for certain cases of granulocytopenia and for certain complications of this disease.

I think one should go further and recommend as a routine treatment for agranulocytosis the combination of pentose nucleotide and penicillin in adequate doses. One has to bear in mind that, according to American authors, the mortality in true agranulocytosis, treated with full doses of pentose nucleotide alone, is still 35 per cent. Liver therapy and blood transfusion have been given up except in cases where the red blood picture is affected. I believe that a further decrease in the mortality rate is possible only with the addition of penicillin, provided that the bone marrow gives some response to pentose nucleotide. The recommendation to employ both drugs is based on the following consideration:—

While the sudden disappearance of the granulocytes may be explained as an allergic reaction to a still unknown antigen, the cause of the fatal issue seems to be an overwhelming

septicæmia due to the absence of the granulocytes, the body's 'first line of defence'. The effect of sodium pentose nucleotide even if given in doses adequate to cause the re-appearance of the granular cells, cannot be expected before 4 to 5 days, and during this critical time even a moderately virulent infection may become fatal. Penicillin, however, will bridge this gap, and will take care of the defenceless tissues until, as a result of the pentose nucleotide treatment, granulocytes re-appear again in normal numbers. If penicillin is not given it is possible that the stimulating effect of the pentose nucleotide even in early diagnosed cases is counteracted by massive bacterial invasion. To delay with the penicillin treatment for the various manifestations of sepsis, which will only become evident with the re-establishment of the normal defence mechanism, means taking an unnecessary risk as vital tissues might be destroyed in the meantime.

The *Journal of the American Medical Association* published in one of their issues of the last year three cases of agranulocytosis treated with pentose nucleotide and penicillin, all of which recovered.

The case recently treated in this hospital is given as a further example for this combined treatment. The previous history leading up to the agranulocytosis is interesting, but the various aspects need not be discussed.

The patient, aged 43 years, had been under dental treatment from the 29th May, 1945. Seven teeth were to be removed for apical abscesses and granuloma. Up to July four teeth were extracted without febrile reaction, but dry sockets developed and the healing was very slow. On the 10th July, 1945, two more teeth were extracted; on the 16th July there was a temperature up to 101°F., and the patient took without medical advice three tablets of sulphonamide. From 17th July to 24th July there was no fever, but healing was again very slow and the patient complained of pain. From 24th July to 25th July he took three tablets of compral (amidopyrine plus trichlorethylurethane). On the 25th July the patient's temperature rose to 102°F. The medical officer found no malaria parasites in the blood but a leucopenia was already noticed, a tentative differential count showing only 7 per cent granulocytes. The following morning the patient was admitted to the hospital. He was in good general condition, temperature 102°F., pulse 100. He complained of headache and of pain in his throat. The tongue was coated, the left tonsil congested showing a small ulceration with whitish margins. The regional glands were enlarged. Heart and lungs N.A.D., spleen was not enlarged. Hæmoglobin 13 gm. (=90 per cent). Red cells 4,850,000. White cells 2,200. Differential count: eosinophils 2 per cent (stab. 1, segment 1), lymphocytes 68 per cent, monocytes 30 per cent.

Penicillin was given intramuscularly at 3-hour intervals, starting with 20,000 units and followed by 12,000 units for the subsequent injections up to a total of 540,000 units. The pentose nucleotide was given intramuscularly in doses of 10 c.cm., 30 to 40 c.cm., daily for 6 days. A total of 210 c.cm. was given.

The ulceration of the left tonsil disappeared on the third day of the treatment, the unhealthy looking gums healed quickly and the patient felt remarkably well with the temperature coming down to normal. The last defective tooth will have to be extracted at a later date under close observation.

My thanks are due to Lieut.-Colonel D. Sanyal, I.M.S., for allowing me to publish this case report and to Mr. G. Winternitz for the laboratory work.

A Mirror of Hospital Practice

A CASE OF SCLERODERMA WITH SCLERODACTYLY

By JOHN LOWE, M.D. (Birmingham)

School of Tropical Medicine, Calcutta

UNDER the terms diffuse scleroderma, sclerodactyly and acrosclerosis is described a group of conditions of doubtful ætiology and rather rare occurrence. Recently a patient with disease of this nature was admitted to the Carmichael Hospital for Tropical Diseases and this case seems worthy of report.

The patient is a Bengali woman, aged 25 years. The disease started nearly two years before admission, with some pain, swelling and stiffness of the right middle finger. The patient, an intelligent woman, describes the subsequent occurrence of pain in the right shoulder region and in the knees. A few months later all the digits of the hands and feet showed affection, and also there was limitation of movement and some pain on movement in the larger joints of the body and also of the spine and the jaw. During these two years the limitation of movement and pain on movement of the small joints of the hands and feet and of some of the larger joints have steadily developed, and during the last six months she has been practically crippled, unable to walk, feed herself, etc.

During the last nine months, however, changes have also appeared in the skin. Pigmented patches first appeared on the back, and the skin was hard, thickened, glossy and scaly. Later were noticed similar changes on the skin of the neck, chest, knees, hands, shoulder, cheeks, etc., and now similar changes are present over most of the body.

On admission the general appearance of the patient was very peculiar and striking. The patient was very thin, weak and emaciated, unable to walk, and she lay on her bed with her knees semi-flexed and her forearms lying across the abdomen with the wrists in marked flexion and the fingers in marked extension, except that the terminal phalanges were slightly flexed. The patient, though bright and intelligent, showed a marked lack of facial expression, a mask-like face.

On physical examination the following points became clear: (1) The occurrence of diffuse scleroderma affecting most of the skin of the body, the skin having a hard, firm, rubbery consistency and a scaly epidermis.

(2) The limitation of movement of joints. The joints of the fingers and the wrists were almost immobile, also the toes and ankle joints. The elbows showed practically no limitation of movement. There was slight limitation of movement of the shoulder joints; the neck was fairly mobile but the thoracic and lumbar spine showed only limited mobility. The hip joints were apparently unaffected and the knee joints, though held flexed, were not fixed but were movable from half to full flexion. They could not however be fully extended. The patient could move the jaw, but not freely and quickly.

(3) The condition of the skin. The surface of the epidermis was dry, smooth and slightly scaly. When felt between the fingers the epidermis felt thin but the

dermis itself in many parts of the body felt thick and hard, with a curious loss of mobility and elasticity. It felt as though the skin, subcutaneous tissue and superficial fasciæ were all involved in the process of induration, and also possibly the superficial muscles, for it was impossible to move the skin over these deeper structures.

(4) Muscles and tendons. The muscles of the forearm were hard in consistency, and the tendons of the wrist were prominent and tense. Similar findings were made in the hamstring and calf muscles, and it appeared that the limitation of movement of the wrist and knees and ankle joints was largely due to this condition of the muscles of the forearm and of the leg. The muscles of the face were also indurated and it appeared probable that this accounted for the limited mobility of the jaw.

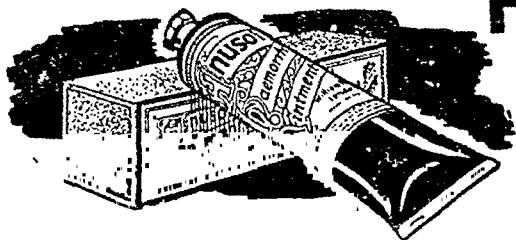
(5) The x-ray examination of the joints showed no condition of the joints themselves which would prevent movement. This added support to the impression that the limitation of movement was caused by extra-articular factors.

Beyond the findings recorded above no other finding of importance was made. The patient is a married woman, married for ten years and had had no children; there is a history of dysmenorrhœa and leucorrhœa; there is a moderate degree of anæmia of macrocytic hypochromic type.

Diagnosis.—During the two years that the disease has been developing, the patient has seen many physicians who have regarded the disease as a multiple arthritis. Numerous forms of treatment have been given, including atophan, milk injections, arsenical injections, vaccines and myocrisin. The patient thought that the milk injections to begin with caused a temporary improvement, but later there was no improvement, and the disease was progressing in spite of all this treatment.

The appearance of the patient would negative a diagnosis of multiple arthritis. The condition of the hands is completely different from that seen in rheumatoid arthritis. Moreover, examination indicates that the limitation of movement of them is caused more by thickening and sclerosis of the skin, subcutaneous tissue muscles and tendons, and that any changes in the joints are secondary to this. X-ray examination of the joints revealed only some rarefaction of the bones.

The condition is well described in the *British Encyclopædia of Medical Practice*, Vol. II, pp. 40 to 42, under the terms scleroderma and sclerodactyly. This description mentions its occurrence in women between the ages of 20 and 40, the occurrence of changes in the skin starting in symmetrical areas of the face, neck and arms, the induration and contraction as the skin becomes harder and immobile until the victim is hide-bound; the mask-like face, the immobility of the mouth, the fixation of the joints in semi-flexion, the fibrosis and atrophy of muscles, etc. This is frequently associated with sclerodactyly affecting the hands and feet, the fixation of joints and later absorption of bones. It is to this condition of the hands and feet that the term acrosclerosis (hardening of the extremities) is applied. It is stated that scleroderma and sclerodactyly are very frequently associated, and in fact are regarded by many as part of the same syndrome, and that the hardening and stiffening of the fingers or else diffuse scleroderma or sclerodactyly may appear first, but they frequently appear simultaneously.



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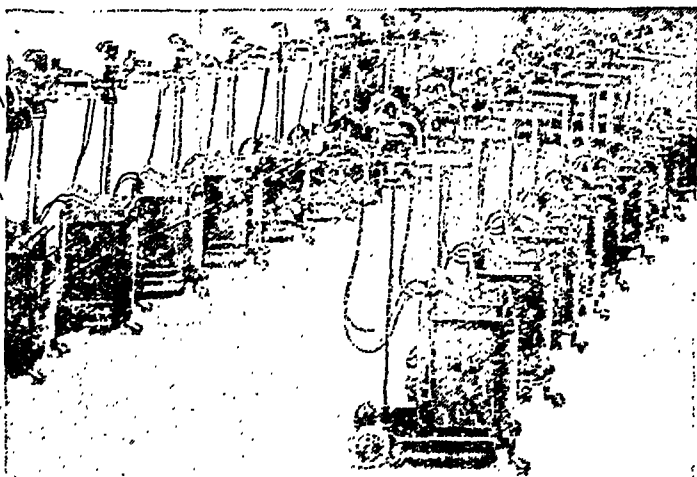
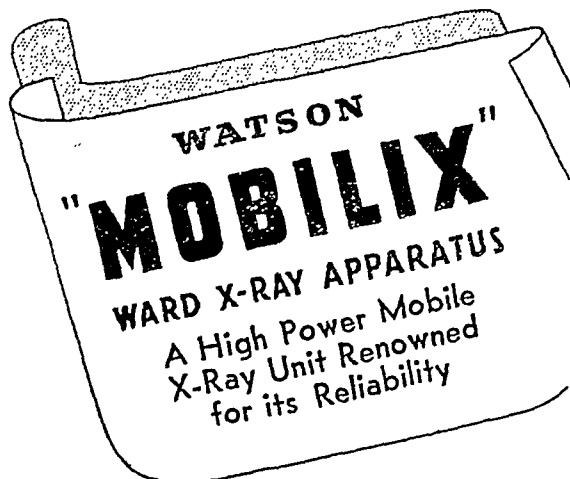
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Indian Medical Gazette

JANUARY

PALUDRINE (M.4888)

For several months now, newspapers, wireless bulletins, and public statements have been making reference to a new antimalarial drug introduced by Imperial Chemical Industries, which was said to be of great potency, and to be a great advance on anything yet available. So far no publication has appeared in the medical press available to us on the subject, and numerous requests for information made to this office could only be answered by the statement that we knew no more about it than is contained in the daily press. Moreover, the Indian agents of I. C. I. knew no more about it than we did. The reasons for this were mainly those of security. It is obvious that an army possessing an antimalarial drug of great potency would be at an advantage, and for this reason, research on antimalarial drugs and information regarding them were kept secret. Even research workers engaged in the work frequently knew little or nothing about the chemical formulæ of the drugs they investigated.

Now the cloud of secrecy is lifting and information is becoming available. We have just received a copy of a statement made by Brigadier N. Hamilton Fairley in Australia a little over a month ago which gives much of the information which we have been seeking. The statement describes how from 1942 English research chemists and biologists working in the laboratories of the I. C. I. succeeded in synthesizing a new series of antimalarial drugs. The early members of the series gave interesting results, but these results were hardly good enough to justify extensive trials in human beings. It was in 1944 that two chemists, F. M. Rose and F. H. S. Curd, synthesized two new drugs which immediately appeared of great promise.

The testing of these drugs in bird malaria was undertaken by Dr. D. G. Davey, and the drugs were found to be potent in destroying malaria parasites of bird malaria. There was, however, a still more striking finding, namely, that the administration of these drugs to birds prevented the infection developing, and it appeared that the drug destroyed the parasites before they developed in the red cell. Such a combination of actions had never been found before in any antimalarial drug. Dr. Davey found that one of the drugs, M.4888, was definitely superior to the other, M.4318, and he demonstrated the causal prophylaxis of malaria in four different species of malaria affecting birds. As Brigadier Hamilton Fairley points out in his note, other researches have shown that an action produced by a drug in bird malaria is not necessarily produced by the same drug in human malaria,

and therefore arrangements were made for clinical trials in malaria patients at the Liverpool School of Tropical Medicine, and later critical experiments on human volunteers were carried out under Brigadier Hamilton Fairley with a special research unit established for the purpose at Cairns, Australia. It is with these researches at Cairns that Brigadier Hamilton Fairley's note deals.

The work consisted of two main parts. Firstly, clinical trials on several hundred patients suffering from malaria acquired in New Guinea. Secondly, a study in two hundred healthy volunteers exposed to malarial infection in connection with research. The work was carried out by a large team of research workers including research physicians, pathologists and entomologists, and the work has now gone on for the best part of a year. The researches were mainly directed to four questions: (a) Does paludrine prevent the parasites of human malaria developing in man; in other words is the drug a true causal prophylactic? (b) Does paludrine control an attack of malaria readily and with safety? (c) Does paludrine eradicate a malarial infection? (d) Does paludrine prevent malarial carriers conveying infection to important vector mosquitoes? In his note Brigadier Fairley attempts to answer these four questions.

Regarding the first question, 'Does the drug prevent the parasites of malignant tertian and benign tertian (*P. falciparum* and *P. vivax*) malaria developing in man', the answer appears to be, for *falciparum* 'yes', for *vivax* 'no'.

The prophylactic action of paludrine on *P. falciparum* seems to be marked. It is stated that if three tablets are swallowed three hours before a volunteer is bitten by ten heavily infected mosquitoes, *falciparum* infection does not occur. This is a great advance. Neither quinine nor mepacrine can produce this result. Only pamaquin in a high and toxic dosage can produce this result and even this not always. In the field, one tablet of the drug taken every day will prevent *falciparum* infection developing at all. While under such a regime, a person can be bitten by *falciparum*-infected mosquitoes and the infection is never able to establish itself. Intensive efforts to demonstrate parasites of *P. falciparum* in these patients completely failed, and the injection of large quantities of their blood into other volunteers did not produce the infection.

Thus this action on *falciparum* infection is much more potent and is of a rather different nature from that produced by mepacrine. With suppressive mepacrine, infection can take place and parasites appear in small numbers in the blood from the 7th day, but are destroyed within 3 or 4 days and the infection is cured. With paludrine even this transient infection cannot occur, since the parasites are destroyed at once and not 10 days later. These facts indicate an action of mepacrine on one or both of two phases

of the parasite which probably occur before the erythrocytic phase, namely the sporozoite, and the tissue or exo-erythrocytic phase of the parasite.

With *P. vivax* infection, however, the results in this respect were a little disappointing. Suppressive paludrine, one tablet a day, does not prevent infection. The parasites do establish themselves, although no symptoms appear, and parasites do not appear in the blood. It is only when the drug is discontinued that parasites appear and frank malarial fever develops. Thus the findings with paludrine in vivax infection in this respect are similar to those made with mepacrine, except that with mepacrine the parasites are present in the blood in small numbers, and the blood when injected into a healthy volunteer not on suppressive treatment will produce infection.

The second question, 'Does paludrine control malarial attacks?' To this question the answer given is yes. It destroys parasites just as they are about to multiply in the blood and gives clinical results 'comparable to but in no way superior to those obtained with proper doses of quinine or mepacrine'. The statement says, however, that the smallness of the dose of paludrine required to control an attack of malaria is very remarkable. One single tablet of 0.1 gm. has proved sufficient to end an attack and bring the temperature to normal in falciparum and vivax infections. (This statement is quoted verbatim from Brigadier Hamilton Fairley's report, but it seems not quite reconcilable with the previous statement that one tablet a day will only suppress vivax infection. Nevertheless, it is clear that the action of paludrine in controlling the attack of malaria is extremely potent.)

The third question, 'Does paludrine produce a radical cure of malaria', cannot yet be answered fully. Brigadier Fairley says that, at Cairns, out of 66 cases of falciparum infection 64 were cured by 3 tablets daily for 10 days, and states that this result is superior to that achieved with either mepacrine or quinine in the same period. Nevertheless, all malariologists know that relapse of falciparum infection after treatment is uncommon. Regarding the power of paludrine to prevent relapse of vivax infection, the evidence is much less satisfactory. Of 31 volunteers given 10 tablets a day for 14 days, 5 showed relapse 'to date' (the length of the period of observation is not stated). If such a number of relapses can be seen within what is presumably not a very long period after such a high dosage of paludrine, it appears that the action of paludrine in preventing relapse of vivax infection after treatment is much less potent than was hoped. Nevertheless, Brigadier Fairley states that results at Cairns indicate that the mere taking of one or two tablets each week end will produce complete freedom from attacks of malaria.

Regarding the fourth question, 'Does paludrine prevent malaria carriers conveying infection to

the mosquito', Brigadier Fairley gives some information of a rather curious nature. Paludrine does not damage or kill the sexual parasites in the blood of the carrier, but when anopheline mosquitoes were fed on the blood of carriers taking paludrine, the parasites failed to develop normally in the stomach of the mosquitoes, and the mosquitoes were incapable of conveying malaria to man. These results were obtained while the patients were actually taking paludrine. Brigadier Hamilton Fairley apparently does not state so, but it appears that the action passes off when paludrine is stopped. Therefore, the rôle of paludrine in the prevention of infection of mosquitoes appears to be limited.

Brigadier Fairley summarizes the results of the Cairns experiment as follows:—

'The results of the experiments on experimentally infected volunteers at Cairns and the clinical trials with paludrine in various Australian military hospitals have duplicated in human malaria the results obtained by Dr. D. G. Davey in bird malaria.

Paludrine is superior to all known antimalarial drugs inasmuch as it is a true causal prophylactic in malignant tertian malaria and a partial causal prophylactic in benign tertian malaria. The only other drug which has a similar action is pamaquin; but this drug has to be given in a dosage which is far too dangerous for routine use in man.

Paludrine in therapeutic dosage controls malaria fever and terminates the attack. It produces radical or permanent cure in the dangerous malignant tertian type of malaria. The percentage cure in benign tertian malaria is not yet known, but the Cairns results suggest that where individuals are not cured, the weekly administration of only 1 or 2 tablets would probably control relapses indefinitely until cure was attained.

Undoubtedly, paludrine is a triumph for British chemotherapy and is the greatest antimalarial drug known.'

The editor has had the opportunity of discussing paludrine with Dr. D. G. Davey who was responsible for the preliminary investigation of the action of paludrine in birds, and who has visited the research centre at Cairns and seen all the results there. Dr. Davey states that the margin of toxicity with paludrine is very great, and wide latitude regarding dosage is possible. He states that it may be possible to control an attack of malaria with a single dose taken on a single occasion; the size of the dose however is not stated. It appears that the ordinary course of treatment of malaria with paludrine will probably last a few days, and will include a number of doses. In the work at Cairns, the ordinary course of paludrine apparently was 3 tablets a day for 10 days. Dr. Davey appears to suggest that a course of this duration might not ordinarily be necessary, particularly in people with immunity to malaria. Regarding the cost of treatment with paludrine, Dr. Davey states that it is proposed to put the drug on the market at a price which will compete favourably with the present price of mepacrine. At present, mepacrine costs half an anna per tablet and a course of 16 tablets costs eight annas. The cost of a course of paludrine will not be greater than this. Moreover, paludrine is stated to produce no unpleasant

or toxic effects whatever in ordinary doses; this cannot always be said of mepacrine. Dr. Davey states that paludrine can, if necessary, be given by injection, but that when given by injection its action is not more rapid than when given by the mouth.

At present no supplies of this drug are available for civilian use in this country, and it is believed that supplies will not be available for several months. Before supplies become available, it ought to be possible to give more detailed information regarding its use. The information given by Brigadier Fairley and Dr. Davey however indicates clearly that a big advance in the therapy of malaria has been made. Moreover, it is not impossible that other members of this series of drugs or of other series of drugs may be better still. The new drug would appear to solve many if not most of the problems of falciparum malaria; it can be prevented, it can be suppressed, it can be cured, and the relapse rate is exceedingly low. The new drug however does not solve the problems of vivax malaria, although it may minimize them; vivax malaria cannot yet be prevented; it can be suppressed; the attack can be terminated readily; but relapse remains a big problem.

J. L.

PENICILLIN THERAPY

THE triumphs of penicillin treatment are now well known, and penicillin is undoubtedly a landmark in the history of medicine. There are, however, three marked limitations of penicillin therapy. The first is its high cost; the second is its rapid excretion, and the third is its limited action against gram-negative organisms. Only the second of these limitations can be discussed here.

In order to maintain an adequate therapeutic blood level of penicillin, it is necessary to give the drug by injection every three hours. This is very trying for the patient and for the medical attendants. Many attempts have been made to overcome this difficulty. The attempts were mainly along three lines. The first line has been to try to give penicillin orally, the second has been to reduce the rate of liberation of penicillin from the site of injection, and the third has been to reduce the rate of excretion of penicillin by the kidney. We will here discuss briefly these three methods.

Penicillin is apparently destroyed by the acid of the gastric juice. Various attempts have been made by various workers to overcome this difficulty by the use of antacids during the period of oral administration of penicillin. Some success has been attained, but the dose of penicillin for oral administration in order to establish and maintain a sufficiently high therapeutic blood level is considerably greater than the amount needed for intramuscular injection. With the high cost and the present shortage of

supplies of penicillin, the oral administration of penicillin is unlikely to be widely applicable.

Attempts have been made to prolong the action of each injection of penicillin by mixing with it some substance which will cause delayed absorption from the site of injection. Various methods have been tried. Penicillin has been given with gelatin, or with vasoconstrictors. It has been given with oil, or in a water in oil emulsion, or with other substances designed to delay absorption. Vasoconstriction at the site of injection has been attempted by the incorporation of adrenalin in the injection. Even the application of ice-bags to the site of injection has been tried. One method about which several articles have been written is the incorporation of penicillin in a mixture of beeswax and peanut oil. Other attempts along similar lines have been the use of penicillin in the form of esters, or of combinations of penicillin with proteins. None of these methods is entirely satisfactory. The method about which much has been written has the mixture of penicillin 100,000 units in 1 c.cm. of 4 per cent beeswax in peanut oil. By such a method some workers have claimed to cure gonorrhœa by a single injection of 100,000 or 150,000 units. Other workers have failed to verify these findings. Studies of the blood level attained by injections of this kind indicate that the delayed absorption from the site of injection does maintain the therapeutic blood level for a considerably longer period than does the ordinary injection, but injections have still to be given 2 or 3 times a day, and the amount of penicillin needed for the 24-hour period is several times as great as that needed for ordinary injections. By these methods, therefore, it is possible to reduce the number of injections in 24 hours, but at the same time the amount of penicillin needed is much greater.

An attempt has, therefore, been made to tackle the problem in another way, to reduce the excretion of penicillin by the epithelium of the kidney. Some workers have used diodone intravenously and have observed a reduction of excretion of penicillin. Other workers with the same object have used para-amino hippuric acid intravenously, and it appears that this substance will increase the blood concentration of penicillin between 2 and 4 times. Other workers have given benzoic acid by mouth and penicillin intramuscularly. The benzoic acid is changed in the liver to hippuric acid which reduces the excretion of penicillin in the urine. The rise in the penicillin content in the blood is, however, influenced by the intake of water and salts. The action of benzoic acid, however, in preventing the excretion of penicillin by the kidney, is a very temporary one, and in order to maintain good therapeutic blood levels, injections have still to be given every 2 or 3 hours, and in addition the benzoic acid by mouth. The method of giving para-amino benzoic acid by injection with penicillin would seem to be

better, but these injections have to be given by vein, they are large in amount, and there is a tendency to the development of oedema. Moreover, this work has been done mostly in animals. A few experiments in man have, however, been made.

Further work is being carried on by various workers along these lines, but at the present time there is no satisfactory and economic method of reducing the number of injections needed for proper penicillin therapy.

J. L.

Special Article

THE BLOOD-BANK AT THE TATA MEMORIAL HOSPITAL, BOMBAY

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MEDICAL men who have worked in general or special hospitals during the war are anxious to apply the knowledge gained by them to work in civilian practice. Remarkable progress has been made during the war years in the use of stored blood and its derivatives for the treatment of several diseases, mainly as a result of organizing 'blood-banks' in many institutions. The literature on the subject is voluminous but scattered, and not easily available in the country. Recently two admirable books have appeared [Kilduffe and DeBailey (1942); Wiener (1943)] which are replete with information which would satisfy even the most curious. It has, however, been our experience that most men associate the running of a successful blood-bank with complicated and costly machinery and large and highly specialized technical staff. This is probably due to the publicity given to large blood-collecting, plasma or serum-desiccating organizations, and to a wrong use of the term 'blood-bank'. A few years ago an eminent physician was addressing a gathering of wealthy citizens. The printer, with a humour peculiar to his profession, had shown the subject of discourse on the programme as 'blood-tanks'. The audience were eager to hear about some new war weapon invented by the laboratories, and heard a learned discourse on what could appropriately have been described as a blood-tank.

A blood-bank is an organization for obtaining suitable blood and distributing it to patients. It is not designed for storing large quantities of plasma or serum in liquid, frozen or dried condition. It owes its success to a rapid circulation and a judicious utilization of small credits and debits. A money bank would run into difficulties if it hoarded most of its assets, and many blood-banks have failed for want of a steady supply of donors and a proper use of stored blood. During an emergency, a blood-bank saves much anxiety to the staff who have to give a transfusion in a hurry. The blood has been collected, typed and stored in the course of the normal working hours by a trained staff, and its use is thus made much easier.

The usefulness of a bank is very much increased if arrangements are made for storage and replenishment of small quantities of liquid or dried plasma which could be immediately administered. This is effected by pooling plasma (with aseptic technique) from bloods which have not been used within ten days, and also by integrating the functions of the blood-bank with those of plasma processing institutions. The preparation of dried plasma should be restricted to a few central organizations which should receive an amount of raw material equivalent to the plasma issued out by them. A hospital blood-bank could not be considered to be operating efficiently if it is required to store blood for periods in excess of a couple of weeks. The equipment and organization for this purpose could be the simplest of its kind and within reach of most well-run hospitals.

It is thought that the actual experience of a small sixty-bed hospital in this matter may be worth recording as an aid to other institutions which may be desirous of starting blood-banks for their own use.

Soon after the opening of the Tata Memorial Hospital it was found that a number of patients admitted for treatment needed blood or plasma transfusion either for building up their general condition before a major operation, or for controlling the after-effects of shock during and consequent on such a procedure. In Bombay, the arrangements for obtaining donors were complicated and unsatisfactory. A small blood-bank was therefore started at the hospital on 21st May, 1941. The equipment consisted of a separate medium-sized refrigerator, twenty Baxter transfusion sets, a Barnstead still for the supply of double distilled water, and other small apparatus usually available in a modern laboratory. A small quiet room was set apart for the bank. The special staff employed was a trained technician and a laboratory boy. No other duties were assigned to these two people. It was arranged that the same operations were performed by the same person as far as possible. The part-time services of one surgeon and one pathologist were available for supervision and storage of blood and for the recording of laboratory data. In retrospect, after four years of work, it is felt that the employment of one full-time medical man for the blood-bank would, certainly have increased the efficiency of the unit, particularly if the pooling

of plasma or serum is to be carried out in a satisfactory manner. The existing unit has however proved adequate for the purpose for which it was started, and it is believed that it has been helpful to many patients who would otherwise have been deprived of the benefits of surgical treatment.

TABLE I

	1941	1942	1943	Total
Number of donors	237	306	274	817
Number of bloods transfused.	168	220	190	578
Plasma transfused in litres.	7	8	10	25

The methods employed and the experience gained by us during these four years are briefly recounted below, with the object of supplying information which is often asked of us. No claim to originality can be made either for the methods which have been in use at this hospital or for the stray observations which have been made during the course of our work.

There is one current misconception which may be worth while rectifying at this stage. It is widely believed that blood or plasma transfusion was an essential wartime requirement for the care of the wounded, and that it should be of minor importance during civilian practice. It is true that traumatic surgery happily plays a secondary rôle in peacetime, but actually, the usefulness of transfusions is as great for ordinary patients in hospital. Whitby (1945) has pointed out that a city of some 499,000 inhabitants between June and September 1944 used nearly 4,000 pints of whole blood and 3,000 pints of plasma (representing a total donation by 12,000 persons) in its 4,000 beds on civilian patients alone, and that a third of these transfusions was used in maternity cases. The physicians, surgeons and obstetricians have witnessed the impressive results of this therapy on their patients, and expect to employ it in future. It is hoped, therefore, that there will be no relaxation of effort to ensure a constant stream of donors in peacetime as in war.

I. The collection and transfusion of blood.

(a) *The procurement of donors.*—The blood for the bank is almost entirely collected from relatives and friends of patients. This work is the responsibility of the medical staff and is not delegated to nurses or the technicians. In the early days it seemed almost impossible to find donors from among the motley crowd of sympathizers who hover round the patients in India during visiting hours. It was gradually found that an intelligent blending of tact, persuasion and firmness was followed by results beyond our preconceived ideas on this, as on many other matters. The clinical staff was prepared to spend considerable time in this work, and practice made them proficient in securing

a regular supply of blood for the bank. Sometimes a suggestion that it would not be possible to treat or operate unless a certain amount of blood was donated to the bank was sufficient inducement. The essential condition however appeared to be that no person should have his skin pricked more than once, because if the blood is taken first for laboratory investigations, the prospective donor generally failed to show up for blood collection. It is likely that we have been particularly fortunate in some respects, and that our methods may be unsuitable for other institutions. The underlying idea in a blood-bank is elasticity, and the details could be modified to suit the needs of different institutions. In a medical school for instance, the junior staff and students are usually willing to donate blood, and should be paid the same amount as any other voluntary donor. As an alternative, a panel or register of donors on the lines suggested by Pons (1939) may meet the requirements of small hospitals. The exuberance of society people and the zeal of social workers may be canalized for the organization of an efficient blood-bank in a particular area. The system of obtaining donors at the Tata Memorial Hospital presented two occasional difficulties which had to be solved. Most of the difficulties were usually overcome by obtaining at least two donors for every patient, irrespective of his immediate needs and by always supplementing the stock in case of paying patients from one of the transfusion services in the city.

(b) *The collection of blood.*—All blood for the bank is collected by the closed method. The prospective donors are questioned about recent illness with particular reference to allergic, contagious, debilitating and parasitic diseases. A brief but careful clinical examination, particularly of the cardiovascular and respiratory systems, is carried out in all cases. This information is recorded on a separate sheet. A person is usually rejected as a donor if an inspection of his cubital fossæ shows thin and inconspicuous veins, if he looks pale and anæmic, weighs under 100 lb. or has donated blood less than two months previously. The selected donor is taken to an aseptic theatre, and blood is collected with all the precautions employed for minor surgical operations.

Effective cleansing of the skin over the selected vein is a necessary procedure which is often neglected. It is always advisable in our donors to scrub the area for at least two minutes with gauze while washing it with liberal amount of soap and water. This is followed by a careful application of 70 per cent rectified spirit and finally ether. A light sterile dry gauze dressing is applied over the area and the skin is allowed to dry for one half to one hour. The skin is cleaned with 70 per cent alcohol followed by ether just before introducing the needle in the vein. If the cost of chemicals is no serious consideration an application

of 5 per cent solution of acriflavine in 50 per cent alcohol and 10 per cent acetone as recommended by Tinker and Sutton is advisable after the preliminary washing and careful drying with sterile gauze.

The operator scrubs, wears sterile gown, face mask and gloves. These procedures may appear unnecessary, but we have had no occasion to regret, and much to commend our fastidiousness. It is usually preferable to take the blood from a person who has been fasting for over six hours. Unfortunately, the work schedule of the hospital has not permitted an observance of this condition in most cases. An incorrect introduction of the transfusion needle in the vein seems to be responsible for most failures in a smooth and easy blood collection. The technique is simple and most people become adept with little practice, until they come across a difficult case, in which a procedure with a semblance of ridiculous simplicity ends in dismal failure. There is no need to be disheartened with such an incident, as the most skilful have experienced it at one time or other.

A few technical details may be recommended as guides for the inexperienced. A double sphygmomanometer band wrapped round the arm and with the pressure maintained between 40 to 60 mm. of mercury is a decided convenience. The skin is pierced, after slightly retracting it laterally, through a selected spot which has been anaesthetized by an intradermal injection of 1 per cent procaine solution. The small weal does not obliterate the vein, and by entering the vein in two stages, the wall of the vein is saved from unwanted punctures. As soon as the needle enters the vein, its angle with the skin is depressed to 10 degrees, and it is pushed into the lumen until the hub and only a small portion of the needle is left out. It is fixed in this position with strips of adhesive plaster. A short bevel needle (16 to 17 gauge) and a glass adapter between the needle and the rubber tubing are advocated, but it has to be admitted that every person works out a method most suited to himself, and no advice is as efficacious as the experience acquired through patience and practice. When the 450 cubic centimetre mark is reached, the collection is stopped by deflating the arm-band, clamping the rubber tubing near the flask, withdrawing the needle from the donor, and applying pressure over the puncture wound for about five minutes. The blood in the rubber tubing is collected in small glass tubes for a Kahn test, for examination of smears for blood parasites, for complete blood count and for blood group determination.

It is our routine to start blood collection by drawing in 50 c.cm. of sterile 3.8 per cent sodium citrate solution through the needle and the rubber tubing into the receiving flask, with the help of a slight vacuum created by the rubber bulb. A 25 per cent solution of sterile glucose is added at the end, of the collection in a pro-

portion of 10 c.cm. for every 100 c.cm. of blood. The blood is mixed with the fluid by gentle and even rocking of the flask all the time and for half a minute afterwards. Any relaxation in this matter, particularly towards the end, results in an undesirable formation of clots. After the collection of blood, the glass tube and connections are removed, a sterile air vent tube is introduced in the cork inlet, a piece of sterile rubber disc and tinfoil is kept on the rubber cork, and the metal cap is screwed in its place. The bottle is labelled and sent to the bank for storage. It is unnecessary to state that all the manipulations are carried out with meticulous care as regards asepsis. The donor is given a large cup of sugared coffee, and made to lie down for half an hour before leaving the hospital. The removal of 450 c.cm. of blood from our healthy adults is a harmless procedure which lowers the total red cell count and the hæmoglobin value by about 10 per cent. These values are restored to the initial level in about a fortnight in the case of red cells, and in about four weeks for hæmoglobin.

(c) *Transfusion of stored blood.*—It is unnecessary to describe the technique of transfusion with which most medical men should be familiar before graduation or while working as interneers. It may not however be useless to mention our experience on some controversial points.

(i) *Age of stored blood.* It has been found that blood collected and stored as described above could be safely used up to a period of twenty days (Strumia, 1942). It is our practice not to use blood more than a week old but to use it for a plasma pool. Any blood which begins to show an advancing pink zone of hæmolysis just above the deposited cells in an undisturbed bottle is rejected as unsuitable for transfusion.

(ii) *Temperature of the blood.* Blood in the bank is maintained at about $4^{\circ}\text{C.} \pm 2$ (39°F.). By the time it is transfused it warms up to about 20°C. in this part of India. It is used for transfusion without previous warming to body temperature. We have not observed any untoward effects by not warming the blood. It is our invariable routine that blood once taken out of the refrigerator is never returned for storage; we commend this practice, as thawing and freezing is injurious to the preservation of blood.

(iii) *Filtration of stored blood.* It is essential to filter all stored blood before its introduction in the recipient's circulation. Several ingenious devices have been proposed for this purpose. Most of them are unsatisfactory and are apt to be discarded in hospital practice. Transfusing stored blood without filtration is a very dangerous procedure. With aseptic precautions, we simply filter the blood from the bank, through four layers of sterile gauze immediately before use. This method is open to several theoretical objections. We would therefore commend the use when available of a sterile stainless steel sieve 14 cm. in diameter with a 0.2 mm. mesh resting in a funnel, as used at the Massachusetts General Hospital blood-bank. The sieve should be moistened with saline before use to break the surface tension. It would be necessary to have several such sets at hand. The Boston blood-bank keeps 48.

(iv) *Preservation of blood.* Various fluids have been suggested and extensively used for this purpose. The addition of glucose to the citrated blood has been shown to be an essential condition if the blood is to be preserved beyond a couple of days. A fluid which has

been used in Great Britain for thousands of bloods since 1940 consists of :—

3 per cent dihydric trisodium citrate .. 100 c.cm.
15 per cent glucose .. 20 c.cm.

This quantity is used for admixture with 420 c.cm. of whole blood. The 3 per cent citrate has an alkaline reaction (pH 8.5–9) and assumes a brown colour if it is autoclaved with glucose, owing to ‘caramelization’ of the latter. An addition of sufficient acid to prevent this change would simplify blood collection by allowing bottles to be sterilized with the necessary amount of preservative in them. The following fluid for 420 c.cm. of blood (Loutit *et al.*, 1943) deserves extended trial in future work.

Dihydric trisodium citrate .. 2.5 gm.
Monohydric citric acid .. 0.5 gm.
Glucose .. 3.0 gm.
Distilled water .. 100.0 c.cm.

(v) *Storage of blood.* The equipment chosen for this purpose should allow for sufficient space and easy inspection. The refrigerator temperature should never fluctuate more than 2° on either side of 4°C. A 35 cubic foot four-door model is recommended by Diggs and Keith (1939), and a bottle cooler type with top doors by Soutter (1944). It is an advantage to have the compressor unit away from the storage cabinets, and a visible temperature recorder outside them.

II. Indications for blood transfusion.—It is necessary to discuss the conditions which necessitate a transfusion, as we have commonly seen fluids administered parenterally without any reasonable likelihood of their doing any good. They were given ‘too little and too late’ to accomplish any desired improvement.

There are certain elementary principles which underlie the use of blood or its derivatives. The blood carries out its main functions (Beling and Lee, 1941) by preserving a fairly constant volume of circulating fluid (Denis, 1668) by its capacity for carrying oxygen (Diggs and Keith, 1939) by maintaining a difference in the osmotic pressure between the intra- and extra-vascular fluids (about 27 mm. Hg.) ; and (Geiger, 1945) by possessing ephemeral constituents necessary for coagulation, immunity, etc. An average adult in good health possesses about 77 c.cm. of blood and about 42 c.cm. of plasma per kg. (2.2 lb.) of body weight. The hæmoglobin content of young persons in Bombay is shown below :

	Hb. per 100 c.cm. of blood, gm.	Hb. per kg. body weight, gm.	O ₂ capacity per kg. body weight, c.cm.
Male ..	15.5	12.0	16.0
Female ..	14.0	10.8	14.5

The plasma contains about 7 gm. of proteins per 100 c.cm. of blood (albumin 4.6 gm., globulin 2.0 gm.). The albumin exerts nearly four times as much osmotic pressure as the globulin, and is chiefly responsible for retaining the fluid in circulation. When the concentration of plasma proteins is reduced below the normal level, fluid begins to exude out of the capillaries and there is at first a latent, and later

(total proteins below 5.5 gm. or albumin below 2.5 gm.) an apparent accumulation of fluid in extravascular tissues (œdema).

When the volume of circulating blood is reduced as a result of its extravasation either inside the body or outside it, the immediate need is a replacement by a fluid capable of exerting the same amount of colloidal osmotic pressure. Such a loss usually occurs after an injury, a visceral tear or during child birth. In some of these cases where a transfusion of nearly 2 litres (about 4 pints) may be necessary during the course of 24 hours, it is obviously desirable to supplement plasma transfusion by whole blood. Most surgeons have observed that a major operation becomes easier, and that the recovery of the patient from it is accelerated ‘if enough blood be administered to prevent the hæmoglobin being reduced below 70 per cent’. In acute infective conditions and abdominal injuries, fresh blood transfusion appears to help the patient to turn the corner towards an ultimate recovery. In burns and crush injuries the capillary endothelium is probably damaged, and the mechanism controlling the distribution of fluid in the body is progressively disorganized. The plasma seeps into extravascular tissues, and the quantity of circulating fluid is gradually diminished by its seclusion in atonic blood capillaries and venules. A disproportion between the volume of circulating fluid and its vascular bed supervenes, the blood becomes concentrated, and a condition of ‘partly dehydrated blood flowing through waterlogged tissues’ is noticed. The hæmoconcentration is an important and early evidence of threatened circulatory failure of capillary origin. The importance of its timely recognition has been emphasized by Moon (1941) because of its occurrence at a stage when the damage is still reparable by plasma transfusion. Beling and Lee (1941) have shown that transfusions of plasma enough to maintain the hæmatocrit value between 50 and 55 and the plasma proteins at 6 gm. at the sixth, fifteenth and thirtieth hours result in a recovery of the blood capillaries, enabling them to hold back the plasma from draining into the tissues. After 40 hours, it is possible to administer about 900 c.cm. of plasma and restore the volume of the circulating fluid. It may not be possible to carry out laboratory tests in mofussil hospitals, and it has been recommended that 100 c.cm. of plasma should be administered for each area of a burn equalling 1 per cent of the body surface. This area roughly corresponds to the surface covered by the palm of an adult person.

The attending physician is sometimes hesitant about administering blood or plasma transfusion in cases of bleeding duodenal ulcer or ruptured ectopic gestation. It is feared that such transfusion may raise the blood pressure and dislodge a newly formed clot from a recently bleeding vessel. This fear has no basis in fact, as Kordenat has shown in experimental

animals that an increase of 5 to 10 mm. Hg. is unable to move fresh clots, and even a rapid transfusion of 450 c.cm. of blood does not raise the blood pressure more than 10 mm.

The patients who are seen by us at this hospital are usually enfeebled by tropical diseases and weakened by cancer. The hæmoglobin is rarely in excess of 75 per cent, and the proteins 6 gm. per cent. Hypoproteinæmia assumes an importance because of a chronic deficiency of protein intake following on long-continued poverty or disease conditions. Recovery after surgical or radiation therapy is therefore slow and eventful in many cases, unless the hypoproteinæmia is attended to, before and during the treatment. In many famine areas of the country the nutritional oedema resulting from a diminution of plasma proteins becomes a major problem. In a study of 24 undernourished Chinese, Ling (1931) found values of serum proteins between 2.7 to 4.9 gm. The workers in Calcutta have stated that most of the Bengal famine sufferers who were admitted to the hospitals for treatment showed evidence of hypoproteinæmia.

A discussion on the uses of transfusion in anæmia and hæmorrhagic diseases is beyond the scope of the present review, as such cases are outside the purview of our usual work. It should however be stated that the rate at which transfusion is given becomes important in civil practice. In normally healthy persons who need transfusion (e.g. wounded soldiers) for traumatic hæmorrhages, the principal consideration is a quick replacement of the lost fluid. In our patients wasted and enfeebled by chronic disease, the cardiovascular system is definitely impaired; therefore, the rate at which the blood volume is increased assumes vital importance. In our series, one of the cases of death attributed to transfusion showed marked fragmentation of heart-muscle fibres, in a myocardium considerably altered by chronic progressive disease (figures 1 and 2, plate IV). The usual rate of transfusion in most cases is about 40 to 60 drops per minute, or 250 c.cm. per hour. In anæmic patients the rate of transfusion should not exceed 2 c.cm. per kg. of body weight per hour. In more advanced cases the rate should not exceed half the above rate. It is important that the determined rate of flow should be maintained steadily. No acceleration, even for short periods, should be permitted.

III. Hazards of blood transfusion.—The use of stored blood could be perilous in the hands of the careless and the unskilful. A blood-bank needs constant supervision, and there should be no relaxation in the scrupulous care with which the various manipulations are carried out. The hazards have been discussed by Whitby in his Harveian Lecture (1942) which should be carefully read by all persons connected with blood-banks. Transmission of disease by blood-transfusion and the importance of Rh factor after

repeated transfusions would need some comment. Bacterial and parasitic diseases may be transmitted by blood transfusion; though it is likely that such a risk progressively diminishes after storage of blood in the bank for more than 96 hours.

There is a record of at least 68 cases of syphilis in which the disease was communicated to the recipient from a donor before the appearance of a primary lesion, the development of a positive serological reaction or during the seronegative phase of the disease. It should be emphasized that the promises and assertions of a donor should neither be depended upon nor taken seriously. In cases of syphilitic infection transmitted by this method, the recipient develops a vigorous roseolar rash (syphilis d'emblée) within about four to ten weeks. The experimental work from Johns Hopkins Hospital however suggests that there is a definite risk of transmitting the disease from patients with early syphilis.

In India, the risk of transmitting malaria and relapsing fever is not negligible, though it is difficult to devise methods of prevention in a widely infected population. In some recorded cases of malaria, the donor denied all knowledge of having had the disease, and the blood smears did not reveal the presence of parasites. The danger of transmitting virus infections during the prodromal stage (smallpox, influenza, measles) has to be borne in mind.

An absence of Rh factor in the blood assumes significance in two types of conditions: (1) in erythroblastosis fœtalis, and (2) after repeated transfusions. Both of them depend on the frequency with which the Rh factor is absent in a particular population. In the European and American white people about 15 per cent are Rh negative. In American negroes 9.1, in the Japanese 2.0 and in Chinese 0.7 per 100 persons are Rh negative. In Bombay City we found that only 2 persons in 100 were Rh negative (Khanolkar and Sanghvi, 1945).

(A) *Erythroblastosis fœtalis*. It has been found in the U.S.A. that in 90 per cent cases of erythroblastosis fœtalis the child is Rh positive and the mother Rh negative. On the basis of the fact that 15 per cent of the women there are Rh negative, it can be calculated that one out of every ten maternity cases would have an Rh negative mother with an Rh positive child. Actually it is found however that erythroblastosis fœtalis occurs in less than one out of five hundred maternity cases. On the same basis, if Rh negative persons are only 2 per cent* in Bombay and if it is assumed that such persons are evenly distributed in the different communities, probably one in every 60 childbirths will be in an Rh negative mother with an Rh positive baby. If the factors which bring about erythroblastosis are the same in India as in the U.S.A., such an occurrence in the fœtus may be met with in less than once in 3,000 expectant mothers. It is probable that erythroblastosis is even rarer than this in Bombay City. The danger attending transfusion of

* Other workers' figures are much higher.—Editor, I.M.G.



Fig. 1. *Case 1.*—Note the triangular opacity in the left cardiophrenic angle. Left dome of the diaphragm raised.



Fig. 2. *Case 2.*—Note the disappearance of the opacity. Lower lobe has expanded.

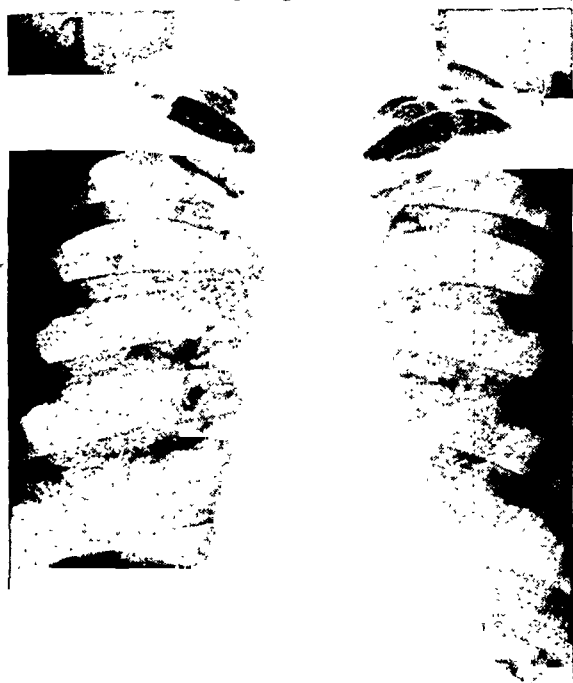


Fig. 3. *Case 2.*—Note the well-marked triangular opacity inside the cardiac shadow in the left side.



Fig. 4. *Case 3.*—Note the triangular opacity in the right cardiophrenic angle. Outline intensified by touching.

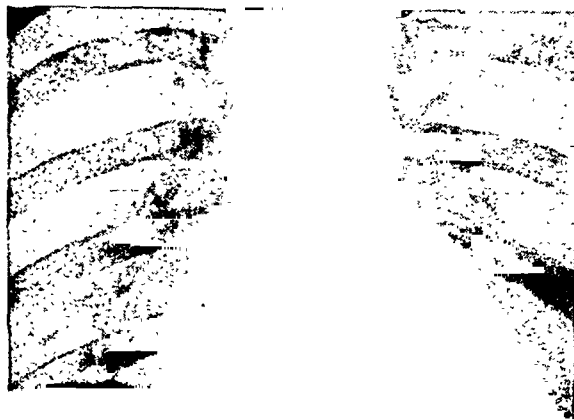


Fig. 5. *Case 3.*—After treatment. Appearance normal.



Fig. 1.—Before treatment.

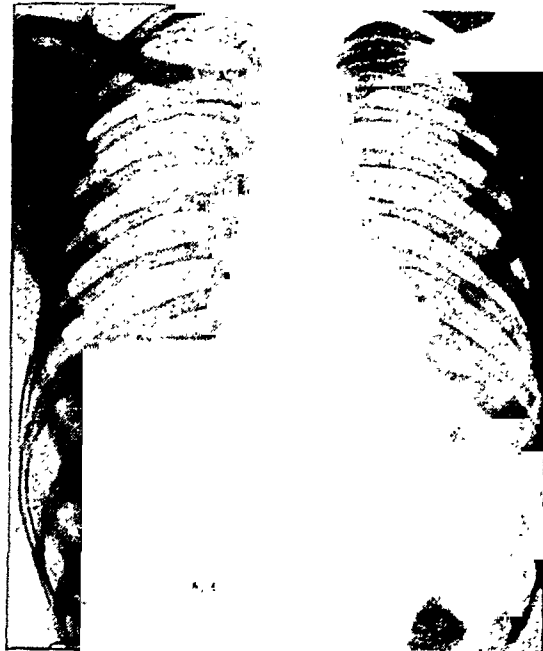


Fig. 2.—After treatment.

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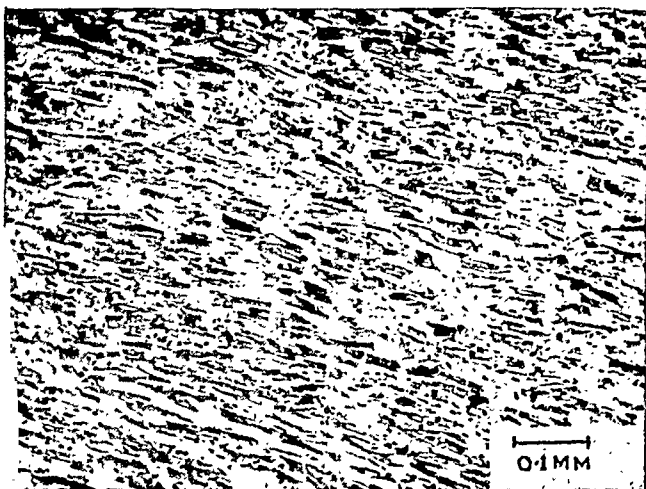


Fig. 1.—Microphotograph of heart muscle ($\times 100$) showing extreme fragmentation and degeneration of the heart muscle fibres; and œdema of the fibro-vascular connective tissue.

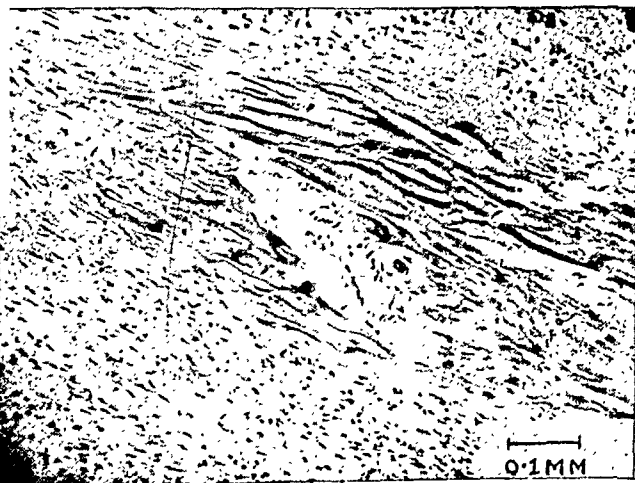


Fig. 2.—Microphotograph of another area ($\times 100$) showing replacement of the heart muscle by œdematous fibrous connective tissue and degeneration of muscle fibres suggesting a chronic myocardial lesion.

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MILITY OF THE ARMS : K. A. SHAH AND
S. B. SHAH. PAGE 10.



Fig. 1.—Photograph of the patient.



Fig. 2.—Radiograms of upper extremities.

Rh antibodies in response to the presence of an Rh positive foetus is evident, but for reasons stated above such an event would be very much rarer in Bombay than in the U.S.A. or Great Britain.

(B) *Hæmolytic reactions due to Rh factor.* Three conditions are necessary for the occurrence of hæmolytic reactions attributable to Rh factor:—

- (i) The recipient should be Rh negative.
- (ii) There should be more than one transfusion with Rh positive blood.
- (iii) The recipient must be able to develop anti-Rh agglutinins.

Owing to the small number of Rh negative persons in Bombay, and a still smaller number of people receiving repeated transfusions, it is likely that the number of such reactions may be negligible here. However, it has to be confessed that there are no data available to us regarding these factors, and it would be unwise to make assertions at this stage of our knowledge.

IV. Transfusion reactions.—Whole blood as well as plasma transfusion is followed in about 6 per cent of the cases by biological reactions which are sometimes very alarming and at others only disquieting. These reactions are of three types:

(A) *Hæmolytic reactions* are rare, about 0.2 per cent, and are due to the administration of incompatible blood (including the so-called universal donor) or unsuitable fluid. The signs and symptoms following such an administration were vividly described by the French physician Denis (1668) nearly 300 years ago and could bear repetition. 'As soon as the blood entered into his veins, he felt the same heat all along his arm and in his armpits which he had done before: his pulse was forthwith raised, and a while after we observed a great sweat sprinkled all over his face. His pulse at this moment was very much altered; and he complained of a great pain and illness in his stomach and that he should be presently choked, unless we would let him go. . . . By and by he was laid in his bed, and after he had for two hours sustained much violence, vomiting up divers liquors which had disturbed his stomach, he fell into a profound sleep about ten o'clock, and slept all that night without intermission till eight o'clock the next day. . . . When he awaked he seemed wonderfully composed and in his right mind, expressing the pain and universal weariness that he felt in all his members. He passed a large glassful of such black urine, that you would have said it has been mixed with soot. . . .

A description of a recent case (Malkiel and Boyd, 1945) with blood from so-called universal donor is also instructive. 'A girl of 19 who had never been pregnant, belonging to blood group A, received 450 c.cm. of citrated whole blood of group O. No untoward signs were noticed during the transfusion, but forty-five minutes after completion of the transfusion the patient complained of a feeling of oppression and had a severe chill. The temperature rose somewhat over 102°F. Jaundice developed, and the icterus index had risen to 62 units within eighteen hours after the transfusion. During the next twenty-four-hour period, oliguria developed. The patient voided only 85 c.cm. of urine during this period, and the urine contained large amounts of urobilinogen. The non-protein nitrogen of the blood was found to be 100 mg. per hundred cubic centimetres at the end of the twenty-four-hour period. Recovery was slow, but at the end of several weeks the patient seemed to have recovered completely from the effects of the transfusion.'

The feeling of discomfort, tightness in the chest, fullness in the head and tingling in the skin may appear very early, after hardly 50 c.cm. have been administered. In any case the transfusion should be immediately stopped and the blood sent back to the bank for bacteriological and laboratory examination. The patient is put on an alkalinizing regime and the blood and urine (24-hour sample) examined for free

hæmoglobin and other blood pigments. Fortunately transfusion of small quantities of incompatible blood does not always result in serious or fatal complications. These are believed to be due to the development of methæmoglobinæmia in patients with low alkali reserves. Administration of 1/6th molar sodium lactate and 4 to 6 per cent sodium bicarbonate solutions has been advised in such cases. The use of 'conditioned blood' in which all agglutinins have been neutralized opens up new possibilities in the use of transfusions.

(B) *Allergic reactions* occur in about 1 to 2 per cent of the transfusions which vary from mild urticaria to severe uneasiness, itching, and collapse. These reactions are usually controllable by a subcutaneous administration of $\frac{1}{2}$ to $\frac{1}{4}$ c.cm. of 0.1 per cent solution of adrenaline.

(C) *Febrile reactions* are unfortunately frequent and are attributable in almost all cases to the presence of pyrogenic substances or other extraneous material in the apparatus or in the distilled water.

It is possible to reduce the incidence of all reactions to a negligible number by an attention to detail and a rigorous technique. A recent report from the Lincoln Hospital blood-bank (Geiger, 1945) is revealing in this respect and the figures are reproduced below:

Total transfusions	1,348
Severe reaction	1
Minor reactions	17
Urticaria	12
Pyrogenic reactions	5

V. Technical problems connected with blood-banks.—The success of a blood-bank depends on the persistence with which an established intelligent routine is observed in all technical procedures. Mishaps, some of them fatal, have been recorded, due to an inadequate care or lack of experience in the grouping of bloods. It is now generally accepted that most febrile reactions are due to improper cleansing and sterilizing of the glassware and rubber parts of transfusion sets, as well as to the use of water containing pyrogenic substances. Chemical cleanliness, and not only sterility of the inner surface of all apparatus, is essential for safe intravenous therapy. A brief description of the routine recommended for the purpose may therefore be useful.

(A) *Blood grouping and cross matching.* This laboratory procedure is an essential part of all transfusion work, as almost all hæmolytic reactions, grave and trivial, are due to administration of incompatible or unsuitable blood. The laboratories connected with a blood-bank should be equipped for undertaking the three following procedures:—

(i) *Titration of testing sera.* The sera used for determining the group (ABO system) should be of high titre. The titre should be ascertained quantitatively whenever a fresh batch is used. We prefer the technique suggested by Wiener.

(ii) *Determination of ABO group.* There is a great variety of techniques recommended for a rapid determination of blood group. It is immaterial which technique is followed, so long as one is fully conversant with it and its limitations. We employ the technique suggested by Greval and Chandra (1940) and are partial to it. It should however be stated that only high-titre sera should be used for the test, and it is always desirable to test the red cells and the serum of the same person separately to avoid a disastrous error. It is also recommended that every test should be checked by a person not performing the test.

(iii) *Compatibility test.* It is advisable to perform a compatibility test just previous to a transfusion.

The open slide method with one drop each of 2 per cent suspension of recipient cells and donor's serum at one end of the slide and another drop each of 2 per cent suspension of donor's cells and recipient's serum at the other end is a quick and satisfactory method when using a donor of the same group. With a universal donor, the technique suggested by Giordano and McBride (1937) is worth further trial.

(B) *Preparation of glassware.* It is desirable to use only non-corrosive glassware, wherever needed (Pyrex, Kimble). New glassware or glassware left unwashed after use (flasks, funnels, etc.), should be carefully washed in running water and immersed overnight in the following cleaning fluid :—

Sodium bichromate	5 gm.
33 per cent sulphuric acid (commercial)			100 c.cm.

Small glass parts, (tubes, adapters, etc.) are cleaned and immersed for a few minutes in the following solution :—

Sodium hydroxide	120 gm.
Water	120 c.cm.
Rectified spirit to	1 litre

The solution is used hot for cleansing purposes.

Rinse thoroughly in running tap water, immediately followed by ten washes with liberal quantities of distilled water.

Drain on clean cloth, assemble and place in heavy cloth bags or wrappings and sterilize *within three hours* of washing. It is better not to use brushes and soaps at any stage of the cleaning process except the first.

(C) *Preparation of rubber tubing, stoppers, etc.* Rubber parts should be of the non-toxic heat resisting variety, which does not stick to glass after use. The rubber tubing should be free from pits, wrinkles and mould marks. It should have a small bore (about 3 mm., 1/8 inch) so that fluids pass through it in a solid column and do not trickle along one side. A good tubing carefully used should withstand about seventy-five sterilizations. It should never be used when it shows any indication of loss of elasticity, as fine fragments of rubber get detached in the lumen.

Dissolve 50 gm. of sodium carbonate in a litre of freshly distilled water. Pour in a clean glass vessel and introduce the rubber tubing gradually in it, so that the solution completely fills the tubing (avoid kinking and contact with metal), cover the container with cloth and place it in an autoclave. Sterilize for half an hour at 15 lb. pressure or at 250°F. Temperatures less than this are unsuitable. Rinse carefully each portion with at least 200 c.cm. of freshly distilled water. Place in a cloth container and sterilize at 15 lb. pressure for 15 minutes.

(D) *Preparation of needles.* Clean needles by drawing a few cubic centimetres of hydrogen peroxide in and out several times. Thoroughly rinse with distilled water; allow to drain in a closed test tube. Irrigate with 2 c.cm. of ether and oil with liquid paraffin and keep with the stylet or wire in position in a test tube with a constriction. Do not sterilize with stylet or wire inside the needles, as the electrolytic action set up between them leads to corrosion and roughening of the inner surface. The needles should be sharpened every time on a mechanical grindstone which maintains the angle of the bevel. This is a small item which adds greatly to the comfort of the donor or the recipient; concerning it we have observed the greatest indifference.

(E) *Care of used transfusion sets.* Immediately after use, all rubber and glass tubing should be rinsed with distilled water and boiled in distilled water, wrapped and stored in a clean dust-free cupboard. They should be autoclaved as soon after their use as the routine of the hospital will permit. Tap water should not be used for cleaning or boiling glass connecting tube, rubber tubing or needles. Fungi or bacteria growing

on dried blood are particularly difficult to remove from the inner walls of the rubber and glass tubes and needles. The inner surface has therefore to be carefully scoured with a detergent solution. The best precaution however is to clean all apparatus carefully piece by piece with clean cold water (never hot) immediately after use, and immediately rinse with a liberal amount of distilled water.

(F) *Distilled water used for making solutions and washing.* The distilled water is single or double distilled in a properly designed still equipped with adequate baffle and trap. The distilled water should be collected in chemically clean glass or stainless steel closed receptacles. It should be used within three hours of its collection for preparing solutions; and the time interval between the preparation and sterilization of solutions should also not exceed three hours. It should be periodically tested for freedom from pyrogens.

Several methods have been suggested for testing the freedom of distilled water from pyrogenic substances. The following three techniques are recommended, though their use depends upon the facilities which are at the disposal of the institution.

(i) *Physical method.* Distilled water is a very poor conductor of electricity and water from a properly functioning still should not show a conductivity higher than 2×10^{-6} mhos at 20°C. If there is some fault or leak in the operation of the still, pyrogenic substances as well as electrolytes begin to enter the distillate. One part per million of chlorine will increase the conductivity by 50 per cent. The conductivity of the water can be easily and quickly tested, and forms an efficient means of testing the water from a still at regular intervals.

(ii) *Chemical method.* 100 c.cm. of distilled water are heated to boiling in a clean beaker and acidified with 10 c.cm. of 10 per cent sulphuric acid. The addition of 0.1 c.cm. of N/20 potassium permanganate imparts a pink colour to the mixture. If, after boiling for ten minutes, the pink colour remains, the sample of water is pyrogen-free.

(iii) *Biological method.* Inject 10 c.cm. into the ear vein of a rabbit which has been previously trained to have rectal temperatures taken without showing marked temperature fluctuations, and determine the rectal temperature hourly for three or four hours. The rabbit's normal temperature ranges from 101.2°F. to 103°F. The febrile reaction which results from the injection of pyrogen raises this to between 105°F. and 107°F.

(G) *Sterilization of apparatus.* It should be clearly understood that boiling glassware, etc., is inadequate for blood-bank work. All apparatus and solutions must be autoclaved. There are certain details in autoclaving which should be always carried out. After inserting the material to be sterilized, the autoclave should be closed and heated or steam allowed to enter with the valve open, to replace all air by steam. The valve should then be closed and heating continued until a pressure of 20 lb. or a temperature of 120°C. (248°F.) is reached. This should be maintained for 30 minutes. Further heating should be discontinued and the pressure allowed to fall to one atmosphere. The valve should never be opened before the fall of pressure to one atmosphere, which usually takes about 40 to 50 minutes. The valve is then opened and the autoclave is emptied a short time afterwards.

VI. *Records.*—The maintenance of careful records has the same significance in a blood-bank as an accurate system of ledgers for a commercial bank. Various forms for recording useful information and indicating the day-to-day position are given in the literature and could be adapted to suit the conditions in any particular institution. The most difficult record to obtain is a statement from the clinic as regards the effects of transfusion on the patient. It

must however be insisted upon in all cases, as it affords valuable guidance to the people working in the blood-bank. A card accompanying each bottle should have information regarding blood flow, reaction, time taken for transfusion, etc., filled immediately by the doctor administering the transfusion, and returned to the bank.

Acknowledgment.—The successful operation of a blood-bank depends on the care and attention to detail by a team of workers. The credit, if any, for the work described above is therefore entirely due to the colleagues in the clinic and the laboratory with whom I have had the privilege of working for the last four years.

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For other details concerning Blood Transfusion Service and Blood-Bank, see this journal vol. 74 (1939), p. 461, vol. 75 (1940), pp. 11, 103, 513, 757, and vol. 76 (1941), p. 413, by S. D. S. Greval *et al.*—EDITOR, I.M.G.

Medical News

CONDENSED M.B. COURSE

A CONDENSED M.B. course at the Calcutta Medical College has been sanctioned by the Government for the benefit of members of the I.A.M.C. and also for the benefit of the medical licentiates of Bengal.

On the recommendations of the Medical Council of India the Calcutta University has introduced a new regulation under which the usual M.B. course of five years six months has been condensed to two years six months in the case of the holders of the L.M.F. diploma and I.A.M.C. personnel who are required to attend a pre-clinical course of six months and a clinical course of two years at a medical college affiliated to the University.

The first batch of medical students started attending the condensed M.B. course at the Medical College, Calcutta, on 1st November, 1945.—Press Note.

INDIAN RESEARCH FUND ASSOCIATION

WE have received a condensed report, in non-technical language, of the Scientific Advisory Board, Indian Research Fund Association, for the year 1944. Some of the important points in connection with the major researches carried out during the year are indicated under the following heads—cholera, malaria, nutrition, leprosy, plague, pharmacology and other researches. For detailed and technical information the original report should be consulted, an abstract of which was published in the October 1945 issue of the *Gazette*.

SHORTAGE OF FOOD IN INDIA

INDIA is faced with a deficit of food grains to the extent of six million tons due to drought in Southern India and absence of winter rains throughout North-West India. The most severely affected area includes several districts in Madras and Bombay Presidencies

and in the Mysore State. Measures contemplated by the Government of India to meet the crisis are: (1) an overall cut of 25 per cent in the basic cereal ration, thus reducing it to 12 oz. with 4 oz. supplementary ration for heavy manual workers; (2) extension of rationing to many more towns in deficit as well as surplus provinces; the total number of rationed towns to-day is 553, but this will soon increase; (3) tightening grain procurement systems in provinces; (4) enforcement of statutory price control. The sale of vegetables is to be subsidized in selected areas, and dried fish is to be utilized as a valuable item of food in scarcity affected provinces by regulating fish exports. Provincial governments have been asked to continue the vegetable production schemes that had been organized for the army, so as to serve the needs of civil markets. A party of officers have gone to ascertain what medical stores and equipment are required in zones affected by food shortage. As a precautionary measure the manufacture of protein hydrolysates has been started at the All-India Institute of Hygiene and Public Health, Calcutta, in order to provide a reserve for emergency.

PHARMACY IN INDIA

A BILL for the establishment of a central council of pharmacy for the registration of qualified pharmacists and provincial pharmacy councils for the regulation of the education of pharmacists was introduced in the central assembly by Mr. S. H. Y. Oulsnam, Health Secretary, Government of India. The bill ensures that persons engaged in the profession of pharmacy have attained a minimum standard of education and training.

As far back as 1931, the Drugs Enquiry Committee, under the Chairmanship of Colonel R. N. Chopra, recommended its early enactment. Since then almost all the pharmaceutical associations and public health bodies have been urging for its early central legislation.

The bill is now circulated for eliciting public opinion.

Public Health Section

THE BACTERIAL CONTENT OF THE CALCUTTA MILK SUPPLY: SUGGESTED MILK BACTERIOLOGICAL STANDARDS*

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and

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Introduction

RECORDS of bacteriological examination of milk in India are very meagre. The first and probably the only attempt at a systematic investigation of the bacteriological condition of milk was made by Joshi (1916) in Bombay. Most of the other milk examinations done in India were to isolate pathogens, for example, Macrae's work (1894) on infection of milk by vibrios, Joshi and Gloster's on tubercle bacilli in milk. In the annual reports of the Health Officer of Calcutta, meagre records of bacteriological examination of milk sometimes occur. In 1919, Ghosh reported an extremely high bacterial content of most of the samples of milk from cows milked in his presence. In 1921, there was a further report by him about the effect of cooling of milk on methylene blue reduction time. In 1932, De (Analyst of the Calcutta Corporation) found the methylene blue reduction test useless as an indicator of the bacterial content of milk. In 1933, Biswas reported the bacterial content of a few pasteurized and fresh milk samples.

In view of such scanty records, work to ascertain the bacteriological quality of the milk supplies in Calcutta was carried out in 1938-39; the present paper incorporates the important findings.

Conditions of the Calcutta milk supply, 1938-39

Out of a total of about 5,000 to 6,000 maunds of milk consumed in Calcutta only about 1,000 maunds were produced locally and the remaining came from the suburbs in trains or buses. About 750 maunds came by train via Sealdah station and about 260 maunds via Howrah station. The supply via Sealdah station came generally from places such as Sodepur, Agarpura, Beliaghata, Shamnagar and Gariahat, but the supply through Howrah station came from more distant places, such as Bansbaria, Bandel and Hooghly. The cows were generally milked very early in the morning from 4 a.m. onwards and the milk reached Calcutta at about 9 a.m., making the interval between milking and collection of samples for examination in many cases as long as 5 hours.

*Paper condensed and rearranged by the editor.

†The work as reported in the present paper was facilitated by the grant of a Maharaja of Darbhanga Scholarship by the Calcutta University in 1938-39 to one of the authors (R. B.).

Multiplication of bacteria in milk

If milk collected under strictly clean conditions is kept cool in a refrigerator, its bacterial content is not greatly increased. Thus a sample of milk which originally gave a plate count of 5,000 colonies per c.cm. gave a count of 16,000 colonies per c.cm. after being kept in the refrigerator for about 24 hours; whereas a sample with an original count of 4,100 colonies per c.cm. gave a count of 720,000 colonies per c.cm. after being kept at the room temperature of 31°C. for 24 hours.

Milk is thus a good nutrient medium for the growth of bacteria, and, as there is a considerable lapse of time between the milking and the arrival of the milk to the consumer, the multiplication of bacteria in it may be considerable, the multiplication being affected by temperature. The monthly temperature records in Calcutta for the year are quoted in the following table:—

TABLE I

Temperature records in Calcutta during 1938

	Maximum	Minimum
January	27.2°C.	14.8°C.
February	27.8°C.	14.5°C.
March	35.8°C.	23.0°C.
April	37.2°C.	26.5°C.
May	33.2°C.	23.0°C.
June	32.2°C.	26.4°C.
July	32.0°C.	26.2°C.
August	31.6°C.	26.1°C.
September	32.8°C.	26.7°C.
October	32.8°C.	23.9°C.
November	28.8°C.	17.8°C.
December	26.8°C.	12.3°C.

It will be seen that the maximum temperature of Calcutta in the summer months, March to October, varied from body temperature to 6°C. below it, and the minimum was always above 22°C. Thus, given the time and the suitable medium, the temperature further favoured the multiplication of bacteria in Calcutta milk as offered to the consumer. The optimum temperature for the growth of most of the pathogens is 37°C., but they are capable of multiplying at temperatures between 17 to 42°C.; so the temperature range in summer in Calcutta was also favourable for the multiplication of these bacteria in milk.

The purpose of the present work

The purpose of the present work was (1) to study the extent of the bacterial contamination of Calcutta milk due to dirty handling, (2) to find out how the dirty handling occurred and to suggest methods for its elimination, and (3) to suggest provisional informative milk bacteriological standards applicable to India.

Collection of samples.—In this work a total of 202 samples of liquid milk was collected for examination, the collections being made partly during summer and partly during winter; the work covered a period of eleven months from March 1938 to January 1939. The sources of the samples were dairies, milk shops, special milk markets, milk stalls, milk-hawkers and *goalas* (vide table II).

TABLE II
Sources from which milk samples were collected

Number of samples.	Summer Winter	Milk shops	Milk markets	Milk stalls	Dairies	Goats and milk-hawkers	202
		17 9 — 26	40 21 — 61	14 6 — 20	42 22 — 64	24 7 — 31	

All the samples were collected between 7-30 a.m. and 9-30 a.m. and generally at about 8 a.m. The samples reached the laboratory within half an hour of collection and were usually examined forthwith. A few samples which could not be examined immediately were kept in the refrigerator but never more than an hour and a half.

For the collection, 100 c.cm. sterile bottles were used. The bottles were provided with ground glass stoppers having overlapping rims to protect the top of the milk from dust particles and from contamination by the fingers during the removal of the stopper. The bottles were sterilized in the hot air sterilizer at 160°C. for one and a half hours.

In collecting a sample, the stopper was removed with the tips of fingers and no inner part was touched. The bottle was then filled with milk and the stopper replaced immediately. When taking a sample from the milk can of the *goala*, the can was shaken and the milk thoroughly mixed. The milk obtained from dairies was in special bottles as sold to consumers. These bottles were closed in a special manner by means of pasteboard and paper, and in some cases sealed to prevent tampering. There were properly covered cans in some of the milk stalls. In the milk markets, the milk containers used by the *goalas* were very unsatisfactory; either these had no covers or if there was one, it was ill-fitting and seldom used.

Leucocyte count of milk.—The cells in milk are mainly leucocytes with a few epithelial cells. The leucocytes occur normally in milk but excess of leucocytes, specially when associated with organisms like the long chained streptococci, indicates unhealthiness of the udder and unsuitability of the milk for consumption.

In 168 samples of milk leucocyte counts were made using the Breed smear method, and the results are tabulated below:—

TABLE III

Ranges of leucocyte counts per c.cm. of milk and the number of samples falling in each

Leucocytes per c.cm.	Number of samples
Under 10,000	6
10,001 to 20,000	8
20,001 to 100,000	43
100,001 to 500,000	78
500,001 to 1,000,000	21
Above 1,000,000	12
TOTAL	168

Savage regards normal variations of leucocyte counts as ranging between 50,000 and 1,000,000 per c.cm. Race

believes that mixed milk containing over 1,000,000 cells per c.cm. should be regarded with suspicion and the supply at once investigated. According to these standards, only about 7.1 per cent of Calcutta milk should be regarded with suspicion.

I. Tests for bacterial contamination of milk

The tests carried out for determining the extent of bacterial contamination were (1) total bacterial count by Breed counting and plate counting, (2) methylene blue reduction test, and (3) 'coliform' test.

Total bacterial count.—The counting in this investigation was usually made by the Breed method,* but as in samples comparatively free from bacteria the method is not reliable, a plate count was also made in such cases. The plate counting was done on the lines recommended by the British Ministry of Health. The agar medium used had 1 per cent of fresh whole milk added to it just before the final sterilization.

The 202 samples of milk are grouped into four classes according to their bacterial counts in table IV.

Thus only 4.4 per cent of milk samples in summer and about 26 per cent in winter belonged to class I having a count of 200,000 organisms and less per c.cm. The average count of 65 samples in winter was 6.86 millions, that of 137 samples in summer was 29.58 millions, and that of 202 samples in the whole year 22.27 millions.

Methylene blue reduction test.—As Baithel Orla Jensen methylene blue which has been used by European workers could not be secured, Grubler's methylene blue was used for this test.

One per cent aqueous solution of the dye was prepared and kept as the stock reagent. Before performing the test, 1 in 10,000 dilution was first made from this stock solution and from that the 1 in 30,000 dilution as required for the test. Ten c.cm. of the well-shaken sample of milk was taken up with a sterile pipette and delivered into a sterile 6 inches × $\frac{3}{4}$ inch test tube. Exactly 1 c.cm. of the 1 in 30,000 methylene blue reagent was added to it. The tube was closed with a sterile rubber bung and was inverted to mix the dye thoroughly with the milk. It was kept at 37°C. Inversion was continued every half an hour up to the maximum period of 5 hours and the time taken for the reduction of the dye noted.

The results of 186 samples tested by this method are given in table V.

The percentages of milk samples which are good in the above classification, i.e. 6 per cent

*For Breed counting, 0.01 c.cm. of milk was taken in a special pipette, spread over one sq. cm. area of a slide, dried promptly in the incubator avoiding contamination, defatted with xylol, treated with alcohol and stained with methylene blue. The slides were examined under a microscope giving a field area of 1/3,000 sq. cm. In counting, a pair of organisms or an aggregated clump of organisms was regarded as one. An organism further removed from a clump than the largest diameter of a constituent individual in the clump was counted separately. The number of fields examined varied inversely with the number of organisms per field; but in any case at least 100 organisms were counted.

TABLE IV
Results of bacterial count in 202 samples of milk

		Number of samples of milk showing, per c.cm., a bacterial count of				TOTAL
		0.2 million and less, class I	more than 0.2 to 5 million, class II	more than 5 to 100 million, class III	more than 100 million, class IV	
Goala	Summer ..	2	13	8	1	24
	Winter ..	1	4	2	0	7
Milk shops	Summer ..	0	2	12	3	17
	Winter ..	1	3	3	2	9
Milk market	Summer ..	1	6	30	3	40
	Winter ..	2	16	3	0	21
Hogg market stalls	Summer ..	0	0	13	1	14
	Winter ..	0	3	3	0	6
Dairies	Summer ..	3	16	23	0	42
	Winter ..	13	9	0	0	22
Totals	Summer ..	6 (4.4%)	37 (27.0%)	86 (62.8%)	8 (5.8%)	137
	Winter ..	17 (26.2%)	35 (53.8%)	11 (16.9%)	2 (3.1%)	65

TABLE V
Results of methylene blue test

[illegible]

in summer and 40 per cent in winter, do not correspond to the percentages classified as good on the basis of the bacterial content. It was found that milk samples reducing methylene blue in 5 hours or more had on an average a bacterial count of 184,300 per c.cm. and 50 per cent of these had a count of below 100,000 and nearly 90 per cent had a count of below 500,000.

The 'coliform' test.—The 'coliform' test has not the same significance in the examination of milk as in that of water. As these organisms are plentiful in the stable environment, in cow manure and in field dust, they are not necessarily indicators of contamination from human sources. They are however delicate indicators of clean milking and proper milk handling.

For this test, milk was diluted 1 in 10, 1 in 100, etc., up to 1 in 1,000,000 and 1 c.cm. of each dilution was inoculated into a MacConkey broth tube, incubated at 37°C. and after 48 hours, tubes showing acid and gas were recorded as positive. The highest dilution giving positive result was recorded as coliform present in the corresponding decimal quantity.

A total of 125 samples of milk were tested for coliform bacteria with the following results :—

TABLE VI
Results of 'coliform test' in 125 samples

Sources	Number of samples in which coliform bacteria were present in milk dilutions of					
	10 ⁻¹	10 ⁻² absent in 10 ⁻¹	10 ⁻³ absent in 10 ⁻²	10 ⁻⁴ absent in 10 ⁻³	10 ⁻⁵ absent in 10 ⁻⁴	10 ⁻⁶ absent in 10 ⁻⁵
Goala	7	3	8	2	2	0
Milk shop	10	0	2	0	1	0
Milk market	11	11	5	3	1	0
Hogg market stalls	6	6	1	0	0	0
Dairy No. 1	1	1	1	3	0	4
" " 2	3	2	4	4	0	0
" " 3	7	3	1	0	1	0
" " 4	8	2	1	0	0	0
TOTAL ..	53	28	23	12	5	4

Besides the above, 10 samples of milk collected directly into sterile vessels from cow's udder were tested for coliform bacteria with the following results : 8 showed absence of coliform organisms in 1 c.cm., 1 showed presence in 0.1 c.cm. but not in 0.01 c.cm., and 1 showed presence in 0.01 c.cm.

The 'coliform' tests were mostly done in summer, a fact which probably accounts for the very unsatisfactory results recorded above. In England, in tuberculin-tested milk, the presence of coliform bacteria in up to 0.1 c.cm. and the absence in 0.01 c.cm. is allowed. Only 4 out of 125, i.e. 3.2 per cent of the milk samples examined, passed this standard. But as 8 out of 10 samples of milk collected under ordinary clean conditions, in sterile bottles, showed the absence of coliform bacteria in 1 c.cm., it is

clear that with proper care much improvement can be effected.

II. The sources of contamination of Calcutta milk

In India, 90 per cent of people are illiterate and so are the *goalas* who are responsible for milking and milk handling. They are ignorant of the elementary rules of hygiene. The methods of production, distribution and sale of milk are all faulty, and bacteria enter the milk at each of the stages as stated below, contaminating it more and more.

During production.—The animals are generally not properly groomed or cleansed before milking. The clothes and hands of the milker are as a rule dirty. There are no regulations to ensure that disease carriers do not handle milk. In adulteration, water of doubtful quality is often used. The milk vessels are not always properly cleansed and sterilization of milk containers is never done by the ordinary *goala*. The cowsheds are usually very dirty, and of a primitive type, specially in the suburbs of Calcutta.

During transport.—Most of the milk consumed in Calcutta comes from out-stations, in

trains and buses. From the distant places it takes as much as 5 hours for the milk to reach Calcutta. In the trains there are no special arrangements for clean transport of this important foodstuff. Special motor vehicles are non-existent. The *goalas* come with their milk in the same compartment with other passengers. The milk cans are not properly covered and often not covered at all. In this unprotected or semi-protected condition, the milk gets infected by droplets expelled during sneezing and coughing by persons sitting nearby. It is exposed to dirt on the train and motor vehicles, and to flies. Further, to crown all, ordinary straw or date tree leaves are put into the milk containers to prevent the milk from splashing

and spilling. Bacterial contamination is therefore repeated and gross.

In the market.—In the markets, such as the Sealdah milk market, the *goalas* invariably expose the milk for sale in uncovered milk cans and there is, immersed in it, straw or date tree leaves as stated above. A customer freely dips his hand in the milk to judge its quality and the milk seller for measuring out the milk. The measuring pot which is dipped in the milk may be left on the floor of the market place when not in use. In short, the contamination that occurs during the daily sale in the milk markets is prodigious, and can only be compared to that of the water of the unprotected village tanks. Final results in the two cases are of course entirely different. Whereas, in the case of water the contaminating bacteria may not be able to multiply greatly, in the case of milk which is a good nutrient medium, the multiplication is rapid and by millions. Conditions in the properly run dairies are much better. In these, properly covered receptacles are used for storing milk. Many dairies also sell milk in small bulk in sterilized and properly covered milk bottles.

The above-described conditions about the production of raw milk and its transport to and sale in the city are based on observations made during the period of the work, and these establish conclusively the fact that raw milk thus coming into the city for sale is definitely not clean milk.

Pasteurized milk in Calcutta.—Some firms in Calcutta sell pasteurized milk. Examinations showed that there was something grossly wrong either in the so-called pasteurization or in the subsequent storage of this processed milk.

Tiedeman and Hohl (1938) state that coliform organisms which are almost invariably present in raw milk seldom survive pasteurization, and that in most instances the presence of coliform organisms in 1 c.cm. portions of pasteurized milk by the presumptive test indicated either improper pasteurization or contamination subsequent to pasteurization.

Out of 21 samples of pasteurized milk examined in summer, 12 showed the presence of coliform organisms to 10^{-6} c.cm., 3 to 10^{-5} , 3 to 10^{-4} , 2 to 10^{-3} and 1 to 10^{-1} c.cm. Out of 7 samples examined in winter one showed presence of coliform organisms to 10^{-3} c.cm., 2 to 10^{-2} , 3 up to 10^{-1} and one showed absence of coliform organisms in 1 c.cm.

Studies of the total bacterial count of pasteurized milk showed that samples from a particular farm gave an average count of 375,000 per c.cm. in winter and 29,000,000 per c.cm. in summer and those from another farm 23,000,000 per c.cm. in summer. It should be noted that no country allows in pasteurized milk a bacterial count above 50,000 per c.cm.

Under such unhygienic conditions of milk production, it is not surprising that only about

4.4 per cent of milk in summer and about 26 per cent in winter contained 200,000 bacteria or less per c.cm. Only about 6 per cent of milk samples in summer and 40 per cent milk in winter reduced methylene blue in 5 hours or more, and only 3.2 per cent of milk in summer showed the presence of coliforms in 1/100 c.cm. and absence in 1/1,000 c.cm.

The pollution which causes this high bacterial multiplication in milk, also exposes it to contamination by pathogenic organisms whenever the milk handlers happen to be carriers of diseases, or the water used for adulteration is dirty. Had it not been the usual custom in the Indian household to boil the milk on receipt of the day's supply the spread of communicable diseases through this vehicle would have been far greater than it is at present. In spite of this safeguard, there is, as the following considerations show, a genuine milk problem in this country:—

1. The high bacterial multiplication leads to the deterioration of the keeping quality of milk, and this means economic loss to milk producers and milk-dealers.

2. The amount of bacteria present in milk is sometimes so large, some tens of millions per c.cm., that if added to the same quantity of clear water, it would make it definitely turbid. It is because milk is an opaque fluid, that turbidity due to bacteria is not noticed.

3. When a highly contaminated milk is boiled, the bacteria are killed, but the metabolic products of such a large number of organisms may cause gastro-intestinal irritation especially in infants.

4. Some people, especially westerners, are in the habit of drinking pasteurized milk and do not like the taste of boiled milk. As sufficient properly pasteurized milk is not available they run the risk of contracting disease by drinking raw milk.

5. Owing to the mishandling of milk, not only raw milk but boiled milk, as sold in restaurants and from sweetmeat shops, is also freely contaminated by bacteria. From the viewpoint of disease-transmission, boiled milk is more dangerous than raw milk, because in the latter, pathogenic bacteria may be outgrown by other organisms which are also present, while in the boiled milk free from other organisms, pathogens gaining entrance can multiply without hindrance.

III. A provisional milk standard for India

India undoubtedly should have her own milk bacteriological standards, and the regulations should be made and so enforced that milk conforms to these standards. What the standards for India should be it is difficult to settle at the present moment when milk throughout the country is produced in far from ideal conditions. For a transition period not longer than 5 years, standards may be framed and made informative but not imperative. During this

period, in every important city in India, the government or the municipality should establish its own dairy farms, where milk, both raw and pasteurized, will be produced under controlled conditions. These farms will prove that the prescribed standards of milk are capable of attainment, and demonstrate all the stages of clean milk production and transport. Regular demonstration classes may be held in these model dairies. The public should also be educated and should be taught to demand a bacteriologically pure milk by the propaganda departments of the government and municipality. When the farmers and the public have thus been properly educated, and milk has actually been produced according to standards for some time in the municipal and government dairy farms, the strict enforcement of the milk regulations and standards can follow.

In England at present there are no standards in terms of bacterial content for raw milk. For pasteurized milk, not more than 30,000 bacteria per c.cm. if tuberculin-tested, otherwise not more than 100,000 bacteria per c.cm. are allowed. In the U.S.A. standards vary in different states. But according to the standard that is frequently adopted, grade A certified milk should not show more than 10,000 bacteria per c.cm. Grade A pasteurized not more than 200,000 per c.cm. before pasteurization and not more than 10,000 per c.cm. after pasteurization; grade B not above 1 million per c.cm. before, and not more than 50,000 after pasteurization. Grade C may have more than 1 million per c.cm. before pasteurization but should not contain more than 50,000 per c.cm. after pasteurization.

The writers feel able to recommend the following provisional standards for India:—

A raw milk (1) should contain not more than 200,000 bacteria per c.cm., (2) should not reduce methylene blue in less than 5 hours, and (3) should show no coliform organisms in 1 c.cm. or less.

A pasteurized milk (1) should contain not more than 10,000 bacteria per c.cm., (2) should not reduce methylene blue in 5 hours or less, and (3) should show no coliform organisms in 1 c.cm. or less.

Summary and conclusions

A total of 202 samples of liquid milk were collected in Calcutta, from milk shops, milk markets, milk-hawkers and *goalas* to ascertain the bacteriological quality.

The average bacterial count was found to be about 22 millions per c.cm. The average count of 137 samples examined in summer was about 30 millions per c.cm., and the average count of 65 samples in winter was about 7 millions per c.cm. Only 4.4 per cent of the milk samples in summer and about 26 per cent in winter showed 0.2 million bacteria and less per c.cm.

Testing for methylene blue reduction, 6 per cent of the milk samples in summer and 40 per cent in winter reduced methylene blue at the end of 5 hours and beyond, and thus were classed as good.

The 'coliform' test was done mainly in summer, and only 3.2 per cent of the samples were

satisfactory, showing the presence of coliform organisms in up to 0.1 c.cm. and their absence in 0.01 c.cm. as allowed in England for tuberculin-tested milk.

If the normal variation in the leucocyte count is regarded as ranging between 50,000 and 1,000,000 per c.cm., then 91.8 per cent of milk samples were satisfactory and only 7.1 per cent of the milk samples suspicious, the count being above one million per c.cm.

The contamination of milk by bacteria takes place during the various stages of its production, transit, and sale, due to dirty handling, adulteration with dirty water, transit under insanitary conditions, in vessels not covered or not properly covered, and due to the dipping into it of extraneous substances such as date leaves and straw, and of hands by customers and sellers in the market place.

Pasteurization of milk in Calcutta is not under proper control, and it gave a total bacterial count sometimes similar to that of raw milk, the average counts varying between 375,000 per c.cm. to 33 millions per c.cm., and coliform organisms being present in 1 c.cm. or less in 20 out of 21 samples.

In India, the milk regulations are defective. Sterilization of milk vessels is not imperative, there are no provisions for bacterial examination of milk for control of bacterial content, nor is there any provision for pasteurization of milk. There are no milk bacteriological standards in India. It is suggested that the defects in the regulations be amended forthwith and milk bacteriological standards set up.

Milk bacteriological standards for India should be fixed after say three to four years' running of model dairy farms by government or municipality and based on the results of bacteriological examination done during this period on milk produced under proper hygienic conditions in those dairies. Provisional standards are suggested.

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Current Topics

The Treatment of Relapsing Malaria

By J. F. STOKES

(Abstracted from the *Journal of the Royal Army Medical Corps*, Vol. LXXXV, August 1945, p. 75)

It must be concluded that urea stilbamine is of no practical value in the treatment of relapsing malaria. It is possible that a prolonged course such as is used for the treatment of kala-azar might be effective, but it is clear that, even if it was, it would be of negligible value in saving man-power.

It is maintained that the only hopeful approach to the problem of relapsing malaria is to search for a substance which is capable of eradicating the parasites lying dormant in the reticulo-endothelial system between clinical attacks. The unpleasant side-effects of stilbamidine argue against its trial on a large scale and deep x-ray therapy is impracticable in war time.

Appendicitis with Emphasis on the Use of Penicillin

By G. CRILE

and

J. R. FULTON

(Abstracted from the *United States Naval Medical Bulletin*, Vol. XLV, September 1945, p. 464)

1. PENICILLIN in large doses (100,000 units every two hours intramuscularly) appears to have a definite effect in controlling peritonitis due to appendicitis or to perforations of the large bowel. This effect is much more striking than that seen with smaller doses.

2. In the majority of cases appendicitis is a self-limited disease that subsides spontaneously and completely after 48 hours.

3. The majority of so-called 'ruptured' appendixes are periappendiceal abscesses which are ruptured during the removal of the appendix.

4. If the appendix has ruptured into the free peritoneal cavity, it is unlikely that operation will improve the patient's chances of recovery.

5. After 48 hours the pathosis of acute appendicitis is subsiding appendicitis, periappendiceal abscess, or localized peritonitis. At this stage serious consideration should be given to the advisability of operating.

6. A series of 1,300 appendectomies with one death is reported.

7. The low mortality rate is attributed to early diagnosis, the youth of the patients, the rare use of cathartics, the liberal use of chemotherapy (especially penicillin), and conservative treatment of many cases of appendicitis seen 48 hours or more after the onset of the attack.

Tests of the Effectiveness of DDT in Anopheline Control

By S. W. SIMMONS

(Abstracted from the *Public Health Reports*, Vol. LX, 10th August, 1945, p. 917)

THE average tenant house can be treated with a DDT residual spray at a cost of about \$1.50 to \$1.75, including labour, materials, and overhead, but exclusive of initial outlay for heavy equipment. The spray can be applied either with a hand-pressure sprayer or with a power machine, and at a dosage of 200 mg. of DDT per square foot of surface area has effected a 60 to 90 per cent mortality of wild mosquitoes in unoccupied houses 20 weeks subsequent to treatment. A residual

toxicity of this duration suggests that one treatment per year might be sufficient in the more northern malaria zones of this country, but two treatments will probably be required in the southern zones.

Residual sprays do not give as effective a kill in occupied houses, not because of lack of toxicity, but due to the large proportion of untreated resting places such as furniture, bedding, and exposed wearing apparel. Treatment of household effects is advised where practical.

Treated wood surfaces exposed to 14 inches of rainfall over a period of 4 weeks effected a 25 per cent kill compared with a 75 per cent kill obtained from control panels. Sunlight alone caused a reduction in toxicity of 10 per cent over the same period.

Apparatus and methods for a critical bio-assay of the lethal effectiveness of treated surfaces both in the laboratory and field are described and illustrated. When applied as a spray at the rate of one-tenth pound of DDT per acre essentially 100 per cent larva kills were obtained. According to the solvent and spreading or emulsifying agent employed, applications may be made as a surface film treatment, a stable emulsion, or as a suspension. No appreciable residual toxicity to larvae has been noted, and laboratory tests have shown that bottom mud inactivates the DDT. Distribution of the DDT-laden mud throughout the water has failed to restore toxicity, which suggests that the DDT actually combines with or adheres to components of the mud.

Materials for effective larviciding with DDT cost less than one-fifth as much as a comparable effective application of fuel oil.

The Hospital Diet

By RUTH PYBUS, O.B.E., S.R.N.

(Abstracted from the *Practitioner*, Vol. CLV, September 1945, p. 156)

Nor only are dietary essentials frequently deficient but the food is often lacking in variety, it is insipid in flavour and unattractive to look at. It is not too much to say that in some cases the recovery of the patient is hindered by this inadequate and unattractive food.

Calories.—It is not sufficiently appreciated that the theoretical caloric requirement for 'bed rest', or for the sedentary man, makes no allowance for the increased metabolic rate in fevers, for the extra nourishment which is required by the patient who is convalescing from an acute infection, or for one who is fighting against a long-drawn-out and debilitating illness. No 'average' caloric requirement can be fixed in cases of acute illness and the patient's powers of digestive assimilation must be considered. Perhaps there is a tendency to overfeed the patient in cases of acute disease of short duration, but the hospital diet is almost always inadequate for those patients requiring hospital treatment for many weeks. The monotony of the diet is an important factor in such cases and this is a common cause of a sub-caloric intake, resulting in loss of weight.

Protein.—It is believed that 1 gm. of protein per kg. of body weight is more than enough to maintain nitrogen equilibrium and to prevent symptoms of protein deficiency in the healthy adult. In cases of illness this modest figure for protein may be inadequate, for a sick man cannot derive sufficient calories from the bulky carbohydrate foods usually given. Moreover, there are many conditions in which generous protein feeding is desirable: for example, in cases of burns, tuberculosis, hypoproteinaemia, pregnancy and lactation. In pregnancy, not less than 1½ gm. of protein per kg. of body weight has been provided. In many cases, the animal protein is almost all derived from milk and that the only cooked 'protein' meal is provided at dinner. Milk, although an excellent source of protein, calcium, phosphorus and riboflavin, is particularly poor in iron and is almost devoid of

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certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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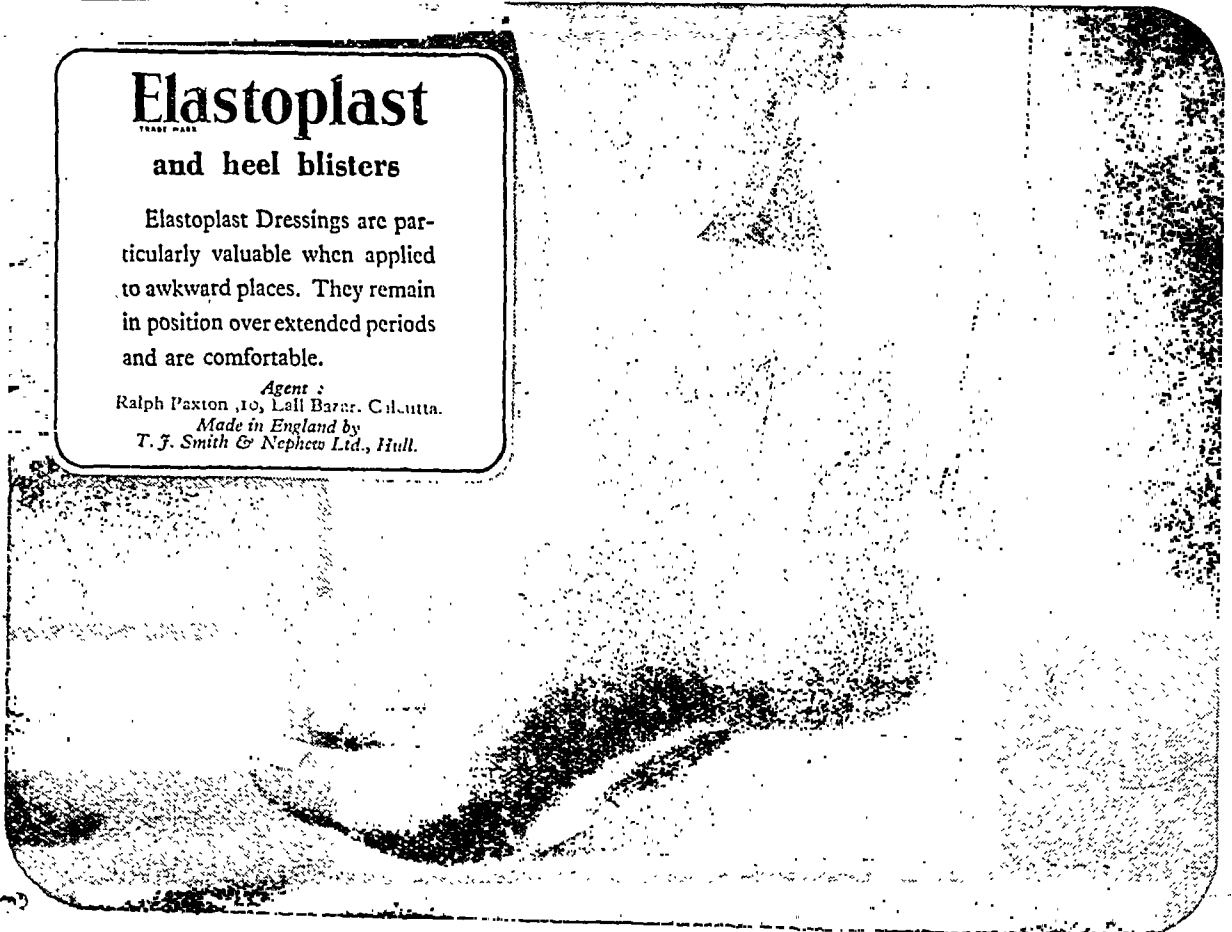
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vitamin C. A plate of fish or meat or egg with a salad or properly cooked vegetable would make up for these deficiencies.

Mineral salts.—In the consideration of a diet the calcium, phosphorus and iron are the only mineral elements which need receive special attention, for if these minerals are present in satisfactory amounts the others will also be well represented. The figures shown in dietary surveys often give a false impression of the adequacy of calcium and phosphorus, for if these minerals are derived chiefly from oatmeal and other whole grains much less will be utilized than if they are supplied from dairy produce—milk, cheese and eggs. The calcium content of cooked vegetables depends greatly upon the calcium content of the water in which they are cooked. This is particularly true of potatoes, which are rather poor in calcium. It may be accepted that if the milk in the hospital diet averages one pint per head and if cheese is used the calcium and phosphorus will be excellent. If less than half a pint of milk is provided these minerals are almost always deficient. In maternity hospitals a special check must be kept on the amount of milk supplied.

The iron content of oatmeal and brown bread is particularly useful and the increased consumption of vegetables in some hospitals has also helped. Eggs are a valuable source of iron.

Vitamins.—The hospital patient requires a generous supply of vitamins, for he has often eaten a poor diet before admission to the ward and his reserves are therefore low. Frequently the powers of absorption are impaired by gastro-intestinal disturbances or by the administration of medicines. The requirements for certain vitamins are increased by fever, infections, the processes involved in the healing of fractures and the repair of wounds, and by various metabolic disorders. The physician or surgeon does not always appreciate these facts, nor does he realize the extremely poor supply of vitamins in the average hospital diet. It should be realized that some 'multiple' vitamin preparations contain inadequate amounts of some of the substances mentioned on the label and it is poor therapeutics to rely on pills and capsules and to provide a badly balanced diet. All the vitamin concentrates on the market may fail to include some of the less well-known, but no less important, dietary factors, whilst fresh fruit and vegetables and dairy produce provide not only vitamins but many other valuable dietary essentials. A pint of milk, two servings of fresh vegetables, a salad or citrus fruit, a good serving of meat or fish, the full use of the fat ration and all available fatty fish, cheese, fresh and dried eggs and liver, a generous supply of potatoes and the inclusion of brown bread, should form the basis of the 'protective diet'.

Unfortunately, the methods used in institutional cooking may seriously affect the natural vitamin content of food, but satisfactory results can only be obtained if the vegetables are cooked briskly for a very short period in a small amount of water, if they are used soon after they are gathered and if they are served immediately after cooking.

Treatment of Subacute Bacterial Endocarditis with Penicillin

By A. L. BLOOMFIELD

C. D. ARMSTRONG

and

W. M. M. KIRBY

(Abstracted from the *Journal of Clinical Investigation*, Vol. XXIV, May 1945, p. 251. As abstracted in the *Journal of the American Medical Association*, Vol. CXXIX, 15th September, 1945, p. 235)

BLOOMFIELD and his associates administered penicillin alone to 11 patients with subacute bacterial endocarditis. These patients had positive blood cultures; their strains of non-haemolytic streptococci were sensi-

tive to penicillin in the test tube; their condition was not desperate and they agreed to stay in the hospital for from six to eight weeks. They were given from 200,000 to 300,000 units in twenty-four hours by continuous intravenous drip for three weeks and thereafter 120,000 to 200,000 units per day in eight intramuscular injections (5,000 units per cubic centimetre of isotonic solution of sodium chloride) for three to five weeks. Most of the patients were treated for eight weeks without interruption. All patients were promptly made 'bacteria free' except one who died early in the course of treatment. Eight were clinically cured of the infection after follow-up periods up to six months. One patient apparently cured of the infection, died of cardiac failure. Cocci were seen in the depths of a scarred mitral valve. There were no clinical relapses or reinfections. Petchiae and emboli continued for some time after the blood cultures were negative. Renal lesions as evidenced by studies of urinary sediment were not as a rule completely eliminated by the treatment.

Chronic Melioidosis

By J. H. MAYER

(From the *Journal of Bone and Joint Surgery*, Vol. XXVII, July 1945, p. 479. As abstracted in the *Journal of the American Medical Association*, Vol. CXXIX, 29th September, 1945, p. 409)

ACCORDING to Mayer, melioidosis is an infective disease occurring in Burma, Ceylon, French Indo-China, the Netherlands East Indies, Malaya and Siam. It is a disease of rodents and men; it is assumed that infection in man is acquired from infected rodents, possibly by contaminated food or water supplies. The causative organism was named *Bacillus whittmori* by Stanton and Fletcher in 1921 but was assigned to the *Pfeifferella* group of bacteria by Topley and Wilson and is now known as *Pfeifferella whittmori* or *Malleomyces pseudomallei*. In most cases the disease has been acute, with symptoms simulating cholera or typhoid, and has proved fatal from septicemia within a few days or weeks. At necropsy the commonest findings have been areas of consolidation and small abscesses in the lungs, and abscesses or areas of caseation in the spleen, liver and kidney. The chronic form of this disease is far less common. The author reports chronic melioidosis in a man aged 33. Some of the lesions primarily involved bone and other cartilage. Much of the patient's improvement may be attributed to the combination of autogenous vaccine and sulphadiazine therapy. An important principle in the treatment of melioidosis is that the abscesses, unlike those of tuberculosis, should be drained early and adequately. Abscess formation was accompanied by a deterioration in the general condition, which improved following the institution of adequate drainage.

Effect of Scopolamine on Airsickness

By J. L. LILIENTHAL

(Abstracted from the *Journal of Aviation Medicine*, Vol. XVI, April 1945, p. 59. As abstracted in the *Journal of the American Medical Association*, Vol. CXXIX, 22nd September, 1945, p. 305)

THE author concludes that scopolamine hydrobromide in doses of 0.6 mg. administered orally thirty to sixty minutes before flight is a potent preventive of airsickness with insignificant side effects.

Ocular Disturbances in Riboflavin Deficiency

By T. D. SPIES, et al.

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXX, September 1945, p. 751)

THREE hundred patients who developed ocular disease after subsisting on diets deficient in riboflavin were selected and treated for brief periods of time

with intravenous injections of riboflavin. There was a prompt elevation in the concentration of riboflavin in the blood and urine. This elevation was rarely sustained for more than a few hours. Within forty-eight hours there was some subjective improvement in all patients, perhaps because they were carefully selected in order to be certain that they had photophobia and were eating a diet low in riboflavin. The degree of improvement volunteered in 80 per cent of the cases was truly remarkable. Within this period there was observed a diminution in the calibre of the dilated vessels in the eye and a striking decrease in the photophobia and corneal ulceration. Accompanying this improvement was a decrease in the number of hæmolytic staphylococci, streptococci, and xerosis bacilli in the exudate from the eyes. Despite the fact that many of the patients included in this study have irreparable eye damage, they are relieved of pain and their vision is improved. Seventy-two per cent of these patients have been able to return to work after months or years of idleness. It is possible, of course, that some of these patients may have severe recurrences and lose their positions. Others may improve slowly and obtain work. We have not followed this group of patients long enough to be certain. These should be regarded only as tentative figures. In fact, we are hesitant about including them at all.

Most of the 300 patients continued to eat their usual inadequate diets with the result that 251 have had recurrences, the first recurrence appearing within from one week to two years after the initial period of therapy. The number of recurrences varied a great deal; a few of the patients have had only one recurrence, and one has had seventeen over a period of two

years. In forty-nine patients there has been no evidence of clinical recurrence as yet, despite the fact that their diets have not improved. In all recurrences the symptoms tended to evolve in sequential order in the same patient, although the variety and severity of symptoms and the order of their appearance varied widely from patient to patient.

The Chemotherapeutic Action of Streptomycin and Promin in Experimental Tuberculosis

By M. I. SMITH

and

W. T. McCLOSKEY

(Abstracted from the *Public Health Reports*, Vol. LX, 28th September, 1945, p. 1129)

THE daily intramuscular injection of 5,000 units of streptomycin for a period of 90 days in guinea-pigs infected with a human strain of tubercle bacilli has produced a chemotherapeutic effect superior to that obtained with 0.5 gm. per kg. promin given orally for the same length of time. Since the dose of promin used is about half the maximum tolerated dose while streptomycin is less than one-twentieth it appears that streptomycin has a chemotherapeutic index better than 10 times that of promin. It also seems possible that by increasing the dose of streptomycin and with better methods of administration its chemotherapeutic effectiveness may be enhanced. Using a suitable combination of streptomycin and promin it was possible to obtain results which, under our experimental conditions, have not been obtained previously.

Reviews

MIDWIFERY.—By R. Christie Brown, M.B., M.S., F.R.C.S., F.R.C.O.G., and Barton Gilbert, B.Sc., M.D., F.R.C.S., M.R.C.O.G. Second Edition. 1945. Edward Arnold and Co., London. Pp. xii plus 831, with 203 illustrations. Price, 15s.

THIS volume is intended to serve as a textbook for pupil midwives, teacher midwives, and obstetric dressers. The authors state in the preface that 'they have attempted to arouse the midwife's interest so that she will not only learn her work but will learn to think clearly about it'. It is noteworthy that the book has been reprinted thrice after its first publication in 1940, and now in 1945 a second edition has been brought out incorporating a brief outline of the history of midwifery and adequate references to the recent advances in the various branches of the subject. The Infants Section is written by a specialist. The book attempts to expound the subject from basic scientific principles; it is written in plain and simple language, and will, therefore, be very useful not only to midwives but also to medical students preparing for midwifery examination.

TEXTBOOK OF GYNÆCOLOGY.—By Wilfred Shaw, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G. Fourth Edition. 1945. J. and A. Churchill Limited, London. Pp. viii plus 636, with 4 plates in colour and 271 text-figures. Price, 24s.

SINCE this book was first published in 1936 it has undergone four editions and two reprints. This fact clearly indicates its popularity among students for whom it is intended.

The author devotes particular attention to the clinical side of gynæcology, laying stress on anatomy and physiology. Detailed pathological descriptions are omitted, but frequent references have been made to standard works. The present edition follows the same sequence as the previous ones; the plates and diagrams are much the same but sixteen new diagrams have been added. The text, however, has been carefully revised and some of it rewritten and brought up to date; new

work on endocrinology and chemotherapy has been included. The book is amongst the best of its kind.

A HANDBOOK OF GYNÆCOLOGY FOR THE STUDENT AND GENERAL PRACTITIONER.—By Bethel Solomons, B.A., M.D. (Dub.), F.R.C.P.I., F.R.C.O.G., M.R.I.A., F.A.C.S. (Hon.), and Edward Solomons, M.A., M.D. (Dub.), F.R.C.P.I., M.R.C.O.G. Fourth Edition. 1944. Baillière, Tindall and Cox, London. Pp. 352, with 280 illustrations. Price, 25s.

THE last edition of this well-known book was published in 1934 and was reviewed in our journal in 1935. In the present edition, Dr. Edward Solomons, a nephew and assistant of the senior author, has become the co-author. Among the important changes brought about in this edition may be mentioned the rewriting of the chapter on anatomy, and that on x-rays and radium in gynæcology by Oliver Chance, the revision of the chapter on the use of hormones, the inclusion of the recent work on leucorrhœa, and ectopic gestation. The chapters on ovarian tumour and on vaginal hysterectomy have been revised. As stated in our previous review, the book is strongly flavoured with the authors' opinions, but these dogmatic opinions are particularly valuable to students when backed by such experience as that of the authors.

THE QUEEN CHARLOTTE'S TEXTBOOK OF OBSTETRICS.—By the Members of the Clinical Staff of the Hospital. Sixth Edition. 1943. Published by J. and A. Churchill Limited, London. Pp. xi plus 577, with 4 coloured plates and 290 text-figures. Price, 25s.

THIS book has been written in order to set forth the views held and the methods practised by those connected with the staff of Queen Charlotte's Maternity Hospital. Something like 1,865 women are delivered in the hospital and 2,200 in their homes in a year. The treatment of puerperal sepsis on a large scale is also carried on at this hospital.

The book is made up of contributions by seven members of the clinical staff of the hospital with the assistance of several other eminent authorities, including the anatomist Professor Frazer who writes on Development and Anatomy. It is divided into ten sections; the first is on development and anatomy, the next six are on the normal and abnormal aspects of pregnancy, labour and the puerperium; the last three are on obstetric operations, the baby, and miscellaneous topics. Each section is presented in a clear, definite and unambiguous manner; unnecessary matter is omitted. The printing is good and the illustrations are excellent and impressive. Since its first publication in 1927, new editions have appeared every three years, bringing it up to date. The present edition includes a small new chapter on post-natal care. It is an invaluable book to students of obstetrics.

RECENT ADVANCES IN OBSTETRICS AND GYNÆCOLOGY.—By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G., and Leslie H. Williams, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G. Sixth Edition. 1945. J. and A. Churchill Limited, London. Pp. x plus 357, with 77 illustrations. Price, 18s.

ADVANCES, according to the authors, are not limited to a set of ascertained facts, even when strung together to make an organic whole, but include any new line of thought penetrating into an unknown region. The authors have, therefore, tried to make the book reflect the current trends of thought and opinion, and their policy is to discard chapters which have appeared in two or three previous editions. The book does not record isolated new facts, but only those which are capable of organic synthesis into a new development, or of modifying and overturning an accepted line of thought on any subject. It has, therefore, been necessary in some cases to quote from papers twenty years old in order to impart to the subject a perspective which illustrates by contrast the present position.

The book is divided into two parts. Part I, 'obstetrics' contains chapters on nutrition in pregnancy and foetal development, vitamin K and hæmorrhagic disease of the new-born, anaesthesia and analgesia in obstetrics, breech deliveries, erythroblastosis, post-natal care, still-birth and neo-natal death, and radiology in obstetrics (written by E. Rohan Williams). Part II, 'gynæcology' contains chapters on cancer of the uterus, sterility, leucorrhœa, sympathectomy, the sex hormones, ovarian tumours (written by Dr. Wilfred Shaw), radiological investigation and diagnosis in gynæcology (by E. Rohan Williams), and x-ray therapy in gynæcology (by W. M. Levitt).

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY.—By Hamilton Bailey, F.R.C.S. Ninth Edition. 1944. John Wright and Sons, Bristol. Pp. viii plus 351, with 492 illustrations, a number of which are in colour. Price, 25s. net

DEMONSTRATIONS OF OPERATIVE SURGERY FOR NURSES.—By Hamilton Bailey, F.R.C.S. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 348, with 531 illustrations, many in colour. Price, 21s. net

HAMILTON BAILEY'S books have a distinguishing excellence of their own, and the two books under review well maintain the reputation.

The eighth edition of 'Demonstrations of physical signs in clinical surgery' was reviewed in detail in this journal in 1942. In the present edition, new pictures have been introduced and old ones replaced, and certain parts of the text have been recast accordingly. We may repeat that 'this book can be strongly recommended to all medical students starting as surgical dressers and to those working for final examinations. A periodical perusal by practitioners would probably enhance the value of their clinical examination and remind them that in diagnosis it is the examination of the patient which comes before other tests such as the laboratory tests and x-rays'.

'Demonstrations of operative surgery for nurses' is a new book, or, more correctly, a compilation of the author's own work with special contributions from twenty-four others including surgeons and theatre sisters. Eighty-three demonstrations of the most modern surgical procedures including sigmoidoscopy are described, for the most part in the form of running commentaries of actual operations. The quality and accuracy of detail of the illustrations conform to the standard usual in the author's books. The author states in the preface that 'Every one of the demonstrations was designed for the nurse herself, and I spared no pains to fill these pages with text and illustrations (over five hundred, many in colour) which I believed even a probationer could understand'. The book will certainly fulfil the great need that exists for a work of this type.

ELEMENTARY ANATOMY AND PHYSIOLOGY.—By J. Whillis, M.D., M.S., F.R.C.S. Second Edition. 1944. J. and A. Churchill Limited, London. Pp. viii plus 280, with 93 illustrations. Price, 15s.

IN the review of the first edition of this book in this journal in 1938 it was remarked that the student commencing his medical course could read this book with considerable advantage as it simplifies and clarifies the two subjects, anatomy and physiology, and at the same time shows where lie the connecting links which are not always obvious in the standard textbooks. In the present edition, the book has been brought up to date by necessary additions, alterations and revision, and a small section on the action of some of the muscles of the lower limb has been added. We would like to repeat that 'It is a book that is particularly suited to the student studying in the smaller medical schools in India and proposing to take one of the lower qualifying degrees, and we recommend this book to teachers in such schools as a class textbook to form a grounding on which they can build. It should also be useful to nurses and others who are not required to go very deeply into the subject'.

THE RADIOLOGY OF BONES AND JOINTS.—By James F. Brailsford, M.D., F.R.C.P. Third Edition. 1944. J. and A. Churchill Limited, London. Pp. xiii plus 440, with 404 illustrations. Price, 45s.

THIS is the third edition of this fine book. The author states in the preface: 'In the ten years' interval which has elapsed since the publication of the first edition of this book, attention has been focused on the recognition of the early signs which characterized the lesions, and, by a careful follow-up of cases throughout their duration sometimes for as long as twenty-five years—the onset and ultimate fate of the affected bones and joints has been determined and some estimate obtained of the time necessary to produce the appearances at any particular stage, and to secure healing and consolidation'. The book covers the subject in twenty-five chapters dealing with the skeleton at birth, hand and wrist, carpus, lower ends of radius and ulna, elbow joint areas, shoulder, bones of the feet, tibia and fibula, knee joint, femoral shaft, hip-joint and pelvis, deformities of femoral head, pelvis, spine, lumbo-sacral and lumbar regions, dorso-lumbar and cervical areas, lesions of the spine, thorax, the skull, the head, developmental abnormalities and dystrophies, generalized diseases of skeleton, changes in bones and joints due to disease and injury, and bone tumours. The book is splendidly illustrated with over four hundred illustrations, excellently reproduced. Authorities are quoted throughout, and there is an excellent bibliography at the end, as well as a good index. In addition to dealing with bones and joints, the book discusses the significance of certain other structures in the soft tissues which by virtue of their relative densities obscure important details or confuse the picture. Reference is also made not only to pathology but also to the treatment of certain conditions of the bones and joints. The book is admirable in every way. It is a mine of information to the

keen clinician and will, we believe, remain an indispensable volume of reference in any radiological department.

CLINICAL ATLAS OF BLOOD DISEASES.—By A. Piney, M.D., M.R.C.P., and Stanley Wyard, M.D., F.R.C.P. Sixth Edition. 1945. J. and A. Churchill Limited, London. Pp. viii plus 138, with 48 illustrations, 45 in colour. Price, 16s.

The fifth edition of this very useful atlas was published in 1942 and was reviewed in our columns in that year. The present edition, in addition to retaining all the good features of the previous one, includes certain essential details regarding magnification of the plates, staining methods, etc., which were not given in the previous edition. As we stated before, the atlas is certainly a useful one to the student and practitioner although its price is rather high.

MEDICAL RESEARCH COUNCIL, SPECIAL REPORT SERIES NO. 252, HÆMOGLOBIN LEVELS IN GREAT BRITAIN IN 1943 (WITH OBSERVATIONS UPON SERUM PROTEIN LEVELS). 1945. His Majesty's Stationery Office, London. Pp. vi plus 128. Price, 2s. net

The nutritional state of an individual or a community depends not only on the availability of foodstuffs but also on hygienic, sociological and psychological factors. Any prolonged deficiency of the two dietetic components, iron and protein, however, will be reflected in the hæmoglobin and serum protein levels; and to obtain some evidence as to the nutritional state of the people of Great Britain in the fourth year of war the Medical Research Council appointed a special committee to co-ordinate surveys of the hæmoglobin and serum protein contents of the blood in representative samples of the population. It was necessary to secure uniformity of technique among the many observers by the use of calibrated apparatus and standardized procedure, and to test the accuracy of the observers in this form of hæmoglobinometry to assess the personal factor.

The present report deals mainly with the hæmoglobin levels of large groups of the general population, but also with a smaller survey of serum protein levels among adults. It consists of the following 12 chapters: Introduction, physiological factors influencing hæmoglobin levels, technical methods and survey procedure, statistical analysis of survey data, comparison of data obtained in the present survey with previous observations on hæmoglobin levels, and with observations made in 1944, the error of hæmoglobin estimation by the Haldane-Gowers method, the effect of constriction on hæmoglobin and serum protein levels of venous and capillary blood, instruments used in previous surveys, estimations of hæmoglobin level in Canadian base troops, the incidence and character of the anæmia in the first 1,000 cases examined for the hæmoglobin survey in the area of the N.W. London blood supply depot, the serum protein level in unselected blood donors in the N.W. London blood supply area, and summary, discussion and recommendations.

The summary of the report is given below:—

Measurements of the hæmoglobin level in about 13,000 adults, including 700 pregnant women, and in some 3,000 children, spread over the period mid-spring to mid-autumn, 1943, were taken. Efforts were made to extend the field of observations widely, particularly with regard to geographical distribution, urban and rural domicile, and to civil state and occupations; but from the nature of the survey, it was not possible to develop it in such a way that it would represent a random sample of the whole population. Many occupations were included, but by no means in the ratio in which they exist in the whole country.

All the observers used the Haldane-Gowers method as recently standardized by the British Standard Institution. This method, though far from ideal, was selected by the committee largely because it is the only one for which a fixed standard of reference—that defined in the B.S.I. specification No. 1079—is available.

By means of this standard, the large number of colour comparison tubes needed by the observers could be provided with their appropriate correction factors. All the pieces of apparatus used in the survey were calibrated at the National Physical Laboratory, and the necessary corrections made in recording the results.

The test for personal errors disclosed the existence of wider discrepancies between the readings of certain of the 60 observers than had been anticipated; this was taken into account in the interpretation of some of the results obtained in the survey, particularly those gained in different geographical and occupational groups.

The comparison of the survey figures with those of earlier surveys and with observations carried out on selected normal groups has been restricted to those made with the Haldane-Gowers method, but even this has proved hard to effect, for the following reasons:—

- (a) The difficulties of preparing and maintaining accurate colour standards in the past have often led to significant discrepancies between the values of the colour tubes used by earlier investigators. Further, colour tubes have sometimes slowly faded or changed in colour during the period of their use.
- (b) The liability of apparatus employed in micro-techniques to inaccuracies of graduation, which, though themselves small, entail high percentage errors in results, has not been sufficiently widely recognized.
- (c) Adequate information about the physiological factors which are known to affect the normal hæmoglobin level is not available in many of the published papers.
- (d) Many of the earlier groups studied were too small to allow definite conclusions to be drawn.

In spite of the difficulty of interpreting the earlier work, it is probable that the average hæmoglobin level of large groups of normal men is known with sufficient accuracy for the present purpose. For various reasons, however, the figures obtained for women and for children in earlier studies cannot be accepted as indicative of normal hæmoglobin levels for these groups. In a large proportion of such studies the individuals examined by earlier observers belonged to sections of the population in which, for economic reasons, the standards of nutrition were undesirably low. In respect of women and children, therefore, the survey suffers from a serious initial handicap which no work on the part of the committee could overcome.

It might be argued that the committee have made the error of reading into their results a degree of accuracy which does not exist. They have been fully aware of the presence of errors, and the statistical analysis has deliberately been limited so as to avoid, as far as possible, the comparison of results which may be seriously influenced by the skill of the individual observer.

The data for men indicate that there is little, if any, difference in hæmoglobin level between married and single; both groups show a virtually unchanging level of hæmoglobin from 20 to 49 years of age. Beyond 50 they show a slight fall, leading to the tentative conclusion that the mean level in man tends to fall slightly in later life, but more observations in homogeneous groups would be needed to substantiate this age trend.

The mean level for hæmoglobin in men obtained in this survey (102) is only a little below the mean value regarded as satisfactory before the war, and the incidence of low values is very small.

The changes in hæmoglobin level with age in women are the reverse of those found in men, the mean value for both single and married women falling slightly in the later part of the age period 20 to 49, but rising again after the age of 50. The fall and rise of the level in women may well be associated with the occurrence of menstruation and with its cessation.

The average values for women are considerably below those for men. A difference of the same order, 8-10 per cent, is seen at all adult ages until 60 and

over; then the fall for men and the rise for women make the curves converge. Whereas the mean hæmoglobin levels for single and married men scarcely differ, those for married women are, at least until the age of 60, roughly 2 per cent lower than for the single women. The evidence suggests that this is due directly or indirectly to the factors involved in child-bearing and rearing.

The mean hæmoglobin values of married women with no pregnancies do not differ appreciably from those of single women, though they are, in general, slightly lower. The married women who have had previous pregnancies differ more widely; their mean values until the menopause being below those of the other two groups.

At every age below the menopause there is a small but consistent decline in the average hæmoglobin level as the number of pregnancies increases. Such changes might be due directly to parturition, or indirectly to a lower nutritional level in the mother as the size of family enlarges. For a given parity, there appears to be no fall in mean level as age advances. The decline with age shown for married women is therefore likely to be due, at least in part, to a relatively large number of women of high parity in the older age groups.

The mean hæmoglobin value for nulliparæ as a whole is slightly lower than that found for the group of students and nurses examined before the war. It is, however, higher than that of a group of Aberdeen women of the poorer class studied in 1935. Serious anæmia is not common, and is definitely less so than in both the Aberdeen group and a group examined in 1942.

In non-pregnant married women under 50 who have borne children, the mean level is rather lower than in nulliparæ. It is therefore definitely below those pre-war figures which, in the committee's opinion, approximate most closely to the normal level for healthy women. It is, however, considerably higher than that of the comparable group of Aberdeen women of low economic status reported in 1935, and the incidence of low hæmoglobin levels is less.

The mean hæmoglobin level for non-pregnant parous married women over 50 years of age is slightly higher than for similar women under 50, but lower than that for nulliparous women over 50. Although below the mean accepted by the committee as satisfactory, the level is higher than the 1935 level for Aberdeen women of comparable age and civil state. Again the incidence of low hæmoglobin values is less than in this Scottish group.

A large number of observations were made on pregnant women attending antenatal clinics. When a broad division is made by the length of pregnancy at the time when the estimation was made, and by the parity of the woman, there is at each given stage no uniform change, except that, as the pregnancy advances, there is—as has been frequently observed—a fall in the average level; slightly lower mean values are apparent during the second pregnancy. A finer division by duration in months, suggests that there may be some truth in the belief that a rise in hæmoglobin level occurs at the end of pregnancy, but the change is very slight and might easily be due to chance with the numbers available. As pregnancy advances, it is noticed that the proportion of women with low hæmoglobin values increases some sixfold.

The figures for pregnant women in the survey compare favourably with the majority of pre-war figures, and with the values available for the period 1940-42. The mean value is, however, lower than that noted for a group of women of a higher average economic level in 1938, and for this reason it cannot be regarded as satisfactory.

A comparison was made between the mean hæmoglobin levels of the wives of Service men and other married women, but at no age was any significant difference found.

The majority of the children under 5 years of age examined in the survey were in wartime day nurseries

in one London borough; hence much caution is necessary in basing any general conclusions on this age group. The infants of 6 months to 1 year have, however, some 6 per cent less hæmoglobin than it would seem possible to attain by iron therapy, and those of 1 to 2 years show equally low figures.

The incidence of anæmia in young children of 2 to 5 years is unduly high.

There is, however, a marked dearth of information regarding the hæmoglobin level of 'normal' children.

When the values for children are reviewed, the general picture is one of a rise from age 1 up to age 6 or 7, followed by a plateau of little change up to age 10 to 11, and then a steady rise. The hæmoglobin level in school boys rises to a maximum at ages 16 to 19, and the girls at the same ages have a value 5 to 6 per cent below that of the boys. Both the mean values are higher than those observed in the under-twenty 'adult class', i.e. those not at school—possibly because the school-children who belong to a higher income group are better fed. At about ages 12 to 13, the girls begin to fall behind the boys. As regards both girls and boys, taking them age by age, no large or consistent difference is observed between the elementary and secondary day schools on the one hand, and the residential preparatory and public schools on the other.

Except at ages 9 to 11, the levels found in the survey for young school-children are above the 1935 Aberdeen levels, and well above figures for London and Edinburgh children obtained in 1942; further, the incidence of low hæmoglobin levels is much less. Taking the age group 8 to 12 as a whole, the survey data indicate no deterioration in hæmoglobin level compared with 1935, and an improvement compared with Davidson's observations for Edinburgh in 1942. Nevertheless, the figures observed in the survey are not to be regarded as optimal. In particular, the observation that boys of ages 8 to 12 at municipal schools show hæmoglobin levels lower than those of the corresponding group at a private residential school, suggests that there is room for improvement.

When the observations are broadly grouped according to the occupations of the tested persons, it is appreciated that, (a) relatively small differences are likely to have little meaning, since the numbers of observations are small, (b) the age distribution throughout the groups is unlikely to be the same, and (c) the differing aptitude of the observers may sometimes have an influence. The most striking feature, perhaps, is the high mean hæmoglobin levels for men in the Civil Service, the Police (mainly Scotland Yard), students, and men in scientific laboratory work; for single and married men, all these groups show high average values, and the proportion with low levels is remarkably small. At the lower end of the occupational scale, there are a few groups with mean values below that of the men as a total group, and with appreciable proportions exhibiting low values. The numbers involved are mainly small, so that undue weight should not be placed upon the smaller differences, but attention may be drawn to certain factory workers and the agricultural workers, both of whom have relatively low average hæmoglobin levels in single and married men. How far these lower values may be attributable to the selective operation of the Military Services Act it is not possible to determine.

With the women, relatively high values are apparent, as with men, in those employed in the Civil Service, and a similar value is given by the large group of W.A.A.F. (mainly new entrants to the Service); of these groups, very few revealed low values. Textile workers had the lowest mean hæmoglobin level recorded by any observer whose readings were not abnormal by the standard matching test: nearly a fifth of them showed low values. A low mean value for the very large group of nurses is also to be noted.

The fact that in adults there was little or no difference between the groups receiving five or more

canteen meals a week plus civilian rations, and those living in civilian rations without such supplements, is at first sight surprising. If food intake alone were the determining factor, one might have expected a noticeably higher figure in the canteen-fed group; on the other hand, it is possible that those who had canteen meals did not take the full share of their rations at home and were therefore no better off dietetically, or that the canteen meals did not necessarily supply the hæmopoietic factors. The whole question, even under rationing conditions, of the value of food depends upon so many factors, many of which are personal and difficult to analyse, that it is not profitable with the evidence available in this survey to suggest the reasons. The fact remains that the taking of canteen meals is not associated with a higher hæmoglobin level. This does not mean that if the group taking canteen meals were deprived of this facility, their hæmoglobin level would necessarily remain at the same level.

The hæmoglobin levels of 990 Canadian soldiers, serving in this country, revealed a mean level some 5 per cent higher than that of the British adult male civilian population of comparable age group, with the exception of two special groups, namely, Scotland Yard officials who are presumably also medically selected personnel, and higher grades of the Civil Service. It is difficult with the information available to assess the significance of this general difference in level, but it is possible that three factors—namely, greater availability of essential foods, increased physical fitness, and medical selection—account to a large extent for the higher hæmoglobin level in the Canadian soldiers. After one year's service there was a significant increase in the hæmoglobin level of these soldiers, and this may be due to the improvement in general fitness brought about by Army training.

Although severe grades of anæmia have rarely been met in this survey, it should be pointed out that in about 7½ per cent of men and women the hæmoglobin levels were below 90 and 80, respectively, which suggests that the efficiency and well-being of these individuals might suffer.

To determine how far iron deficiency might be considered responsible for the incidence of low hæmoglobin levels, a follow-up was attempted of any blood donor found to have a hæmoglobin level below 80, in the first 1,000 examined in one area. The results indicated that the major cause of the low hæmoglobin levels found in the adults studied was apparently a deficiency of iron. Iron therapy relieved the condition.

Serum protein estimations were also made on an unselected group of 353 potential blood donors, or on donors who had given blood not less than three months previously. The range of values found was unexpectedly wide: 5.56 to 7.65 g. per 100 ml., mean 6.560 ± 0.021 g. The mean was lower by 0.215 ± 0.044 g. than that observed in a group of 100 Canadian soldiers serving in this country and living on the British Home Service Ration Scale.

Figures previously recorded in the literature were on the whole in agreement with the values obtained in these soldiers, and this further indicated that the serum protein level of the donors was probably sub-optimal. There was slight evidence that seasonal variation might account for the difference, but this was by no means certain. Other possible explanations are differences in consumption of protein, especially animal protein, by the two groups, and the fact that the Canadians were healthy men, medically selected for service overseas; this was borne out by the high mean hæmoglobin level of the latter.

RECENT ADVANCES IN ANÆSTHESIA AND ANALGESIA.—By C. Langton Hewer, M.B., B.S., D.A. (Eng.). Fifth Edition. 1944. J. and A. Churchill Limited, London. Pp. viii plus 343, with 141 illustrations. Price, 18s.

This book is divided into twenty-six chapters dealing with various topics of the subject. The first chapter

gives a brief account of the theoretical aspects of inhalational anæsthesia and the second, of pre-medication. Four chapters are devoted to nitrous oxide and the hydrocarbon gases, carbon dioxide and helium, ethers, and the halogen containing anæsthetics. The modern apparatus for the administration of the gas anæsthetics and the explosion risk in anæsthesia are dealt with in separate chapters. Endotracheal anæsthesia, intravenous anæsthesia and analgesia, and spinal analgesia are each given one chapter; local analgesia three chapters. There is one chapter on collapse and resuscitation. Then follow seven chapters dealing with anæsthesia and analgesia in neuro-surgery, dental surgery, for endoscopy, nasal and oral surgery including war wounds, thyroid and thymic surgery, thoracic surgery, abdominal surgery, and in obstetrics. The last four chapters are on anæsthetic sequelæ, psychological aspects of anæsthesia and analgesia, oxygen therapy, and anæsthetic charts and records (which is new). Attempts have been made to bring all chapters up to date and references are appended at the end of each chapter.

It is very remarkable, as the author states in his preface to this edition, 'that it has been possible to report on so much new work in so many diverse subjects' so soon after the publication of the fourth edition in 1943. The present edition contains additional information on anæsthesia for thymectomy, general anæsthesia with ethyl chloride and trichlorethylene, intravenous general anæsthesia with procaine, improved apparatus for controlled respiration, pethidine analgesia in obstetrics, pressure infiltrators, fractional caudal block, suction from oxygen cylinders, etc. An excellent presentation of the subject.

GAS AND AIR ANALGESIA.—By R. J. Minnitt, M.D., D.A. Second Edition. 1944. Baillière, Tindall and Cox, London. Pp. vi plus 74, with 18 figures. Price, 5s. net

SMALL books of this type on gas and air analgesia are rare, the method having developed only in this generation. This handbook which contains brief but clear chapters on the history of the method, apparatus and assembly, technique of administration in midwifery, contra-indications and causes of failure, statistics and legislative developments, and applications to minor surgery, will therefore be useful to those concerned with gas and air analgesia. There are also two appendices, entitled 'self-administered analgesia for the midwifery of general practice', and 'research notes'.

PRACTICAL ANÆSTHETICS.—By J. Ross Mackenzie, M.D., D.A. 1944. Baillière, Tindall and Cox, London. Pp. viii plus 136, with 63 illustrations. Price, 10s. 6d.

IN the chapter on 'anæsthetics—to-day and to-morrow'—the author states that 'there is no subject of the medical curriculum in which the student spends less time, and yet in which he is expected to show more proficiency than the theory and practice of anæsthetics'. . . . But the practice of anæsthetics in the teaching hospital and as required by the modern surgical unit does not lend itself to the training of the student in simple methods of anæsthesia'. The author who has a very wide experience of the subject has written this manual for the medical student and the medical or surgical hospital resident.

The book contains twenty chapters, mostly concerning the practical aspects of the subject such as preparation of the patient, premedication and basal narcosis; various kinds of anæsthetic agents, different methods of producing anæsthesia and analgesia, complications and sequelæ of anæsthesia, anæsthesia in infants and children, oxygen and helium therapy. The regulations for the Diploma in Anæsthesia, a summary of the subjects of the examination; a bibliography, and some medico-legal notes are given at the end of the book.

ESSENTIALS OF LOCAL ANÆSTHESIA IN DENTISTRY.—By A. Cornford Bowden, H.D.D., L.D.S. John Wright and Sons Ltd., Bristol. Pp. 60, with 9 figures

IN the introductory chapter the author states that 'no branch of dental practice is more fascinating or of more use to the practitioner than that of local anæsthesia; none calls for more integrated experience or better judgment'. His aim in this little book is 'to give the student a clear, concise view of the fundamental, inescapable facts of local anæsthesia that will help him through his examinations and above all to become a competent, human practitioner even when his main interest is focused on some other branch of practice to which local anæsthesia is merely incidental'. The seven chapters of the book bear the following titles: introductory and explanatory; choice of anæsthetic; instruments and sterilization; drugs and solutions; anatomy; technique; and complications with local anæsthesia; they present the essentials of the subject lucidly and concisely. In his introduction to the book the president-elect of the British Dental Association states, 'When I had read this book I felt I had learned not a few new things and improved my acquaintance with many I had forgotten. If a handbook can have this effect upon one who has been using his syringe daily for a great number of years, then its value to younger men, and those whose knowledge of anæsthesia is empirical only, cannot be questioned'.

LOCAL ANÆSTHESIA: BRACHIAL PLEXUS.—By R. R. MacIntosh, M.A., M.D., F.R.C.S., D.A., and William W. Mushin, M.B., B.S., D.A. Blackwell Scientific Publications, Ltd., Oxford. Pp. 56, with 33 figures. Price, 10s. 6d.

THE object of the authors in this booklet is to remove, by pictures instead of by the written word, one of the disadvantages of local anæsthesia, namely, the uncertainty of bringing the anæsthetic into contact with the nerves carrying sensory impulses from the field of operation. The book contains short sections on history, indications, principles of technique, pre-medication, instruments, local anæsthetic solutions, position of patient, skin wheal, injection of the plexus, onset of analgesia, the stellate ganglion, Horner's syndrome, and complications, each of which is splendidly illustrated.

DIAGNOSIS AND TREATMENT OF DISEASES IN THE TROPICS.—By H. C. Trowell, M.D., F.R.C.P. Second Edition. 1945. Baillière, Tindall and Cox, London. Pp. xiv plus 219, with 35 diagrams. Price, 4s.

A SERIES of booklets were issued for the instruction of dressers and nurses in tropical Africa, and this book is the third of the series. The author was for some years responsible for the training of nursing orderlies in Kenya.

The book is divided into four parts, one entitled introductory, one on surgical diseases, one on medical diseases, and one on special diseases, which includes diets and malnutrition. There are twelve chapters in all, and each chapter gives the necessary facts and information under different headings clearly and simply, and ends with a summary and questions. There are also thirty-five useful diagrams.

CATECHISM SERIES: DISEASES OF THE EYE. Fourth Edition. Pp. 66; **MENTAL DISEASES.** Third Edition. Pp. 84; **VENEREAL DISEASES.** Second Edition. Pp. 80; **PUBLIC HEALTH.** Parts I and II. Fourth Edition. Pp. 132; **PHYSIOLOGY.** Fifth Edition. Part I. Pp. 82. E. and S. Livingstone Limited, Edinburgh. Price, each part 1s. 6d. net

THESE booklets belong to the 'Catechism series' of which twenty-nine books have been published, some in several parts. The questions and answers contained

in this series of books may be of help to students in rapidly revising these subjects. The answers given are accurate, and are written in simple language; each book covers the subject adequately for purposes of the lower-grade examinations in the several subjects. Some of the books are illustrated with diagrams.

OPHTHALMIC NURSING.—By Maurice H. Whiting, O.B.E., M.A., M.B., B.Ch. (Cantab.), F.R.C.S. Fourth Edition. 1945. J. and A. Churchill Limited, London. Pp. x plus 133, with 56 illustrations. Price, 6s. 6d.

Nurses generally pass through their training without having much experience of eye cases. Ophthalmic nursing, however, demands 'a gentleness of manipulation which, though desirable, is not so imperative in other cases'. This little book is based mainly on the practices adopted at Moorfields Eye Hospital, which are the result of more than a century of experience and tradition. In this, the fourth edition, the book is brought up to date; brief notes on the subject of air-raid injuries and burns of the eye, and on virus infection are added. The author, as Sir John Parsons says in the introduction, 'has succeeded in presenting the subject in an admirably concise manner, omitting no essentials, yet at the same time describing and explaining the procedures in a manner comprehensible to those who have had little or no medical training'.

MEDICINE FOR NURSES.—By W. Gordon Sears, M.D., M.R.C.P. Fourth Edition. 1945. Edward Arnold and Co., London. Pp. viii plus 460, with 67 illustrations. Price, 10s. net

THE third volume of this excellent book was published in 1939 and was reviewed in this journal in that year. Since then several reprints of the book have appeared with minor corrections, and now it has been possible to produce a fresh edition in which the book is brought up to date with a number of small additions but without any major alteration. It is simply and clearly written, well covering all branches of medical nursing that the student nurse is expected to know. There are some useful tables.

NURSING IN TIME OF WAR.—By P. H. Mitchiner, C.B.E., T.D., M.D., M.S., F.R.C.S., and E. E. P. Macmanus, O.B.E., S.R.N., S.C.M. Second Edition. 1943. J. and A. Churchill Limited, London. Pp. vii plus 146, with 27 illustrations. Price, 2s.

THIS book is intended for trained nurses entering on spheres of work associated with war conditions. The nine simple chapters on general introduction to air-raid work, nursing in first-aid posts, the conversion of civilian buildings to casualty hospital use, hospitals in huts or tents including nursing under improvised conditions, burns and gas, wounds, shock and infection, fractures, medical casualties, and technique of intravenous transfusion and infusion, anæsthesia, and morphia, will certainly be very helpful to those who have had no experience of the technique and mode of life met with under improvised conditions of war. There are also four appendices giving lists of drugs, dressings, etc., issued to first-aid posts and dressing stations, of lotions, and of some improvisations. In the present edition the book has been carefully revised in the light of practical experience, and several points have been amplified and elucidated.

THE ESSENTIALS OF CHIROPODY.—By Charles A. Pratt. 1945. H. K. Lewis and Co., Ltd., London. Pp. xii plus 156, with 34 illustrations. Price, 10s. net

THIS is a book written for the beginner in chiropody. It contains twenty chapters, of which only the following five chapters are more than ten pages each—the muscles of the leg and foot, which is the biggest containing eighteen pages; flat feet; two chapters on deformities of the toes, one on hallux valgus, and

the other on hallux rigidus, hammer, elevated, and claw toes; and disorders of the nail. The titles of the remaining fifteen chapters are: introduction; the bones of the leg and foot; the joints of the foot; the skin and its appendages; the structure and functions of the arches of the foot; footwear; the principles of treatment; foot hygiene; the essential requirements for chiropody; inflammation; blisters, abrasions and wounds; corns and callosities; hyperhidrosis and soft corns, miscellaneous conditions; and foot inspections. There is also a glossary of technical terms. The illustrations are good. The printing and get-up of the book are excellent, and the book is a good primer for the beginner in the subject.

MASSAGE AND MEDICAL GYMNASTICS.—By Mary V. Lace. Third Edition. 1945. J. and A. Churchill Limited, London. Pp. xi plus 244, with 126 illustrations. Price, 12s. 6d.

This book is intended for teachers and students in training for the conjoint examination of the Chartered Society of Massage and Medical Gymnastics, and the previous editions were based mainly on a translation of 'The technique, effects and uses of Swedish medical gymnastics and massage' by Dr. Arvedson. The present edition has been brought up to date in terminology and in presenting the modern views on rehabilitation.

The teachings are based on sound physiological principles, and the illustrations of massage and exercises are mostly sketched from living models performing the exercises and add greatly to the value of the book. We agree with Dr. Mennell who states in his foreword to the book: 'Only the experienced teacher can realize the students' difficulties, smooth the way for those that come after, and maintain the scheme and the standard from beginning to end. By training and experience Miss Lace is admirably fitted for the task. There has been one aim, and one only, namely to set forth certain essentials that every student must know in a form that will be most readily assimilated, and serve as a clear and solid foundation on which the masseuse and medical gymnast of to-morrow may build'.

BOOKS RECEIVED

1. Aviation neuro-psychiatry. By R. N. Ironside. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 167. Price, 8s. 6d. Postage, 6d. (Home).

2. Handbook of diagnosis and treatment of venereal diseases. By A. E. W. McLachlan. Second edition. Published by E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 371, with 160 illustrations, 20 in colour. Price, 15s. Postage, 7d. (Home).

3. Essentials of surgery for dental students. By J. Cosbie Ross. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 284. Illustrated. Price, 20s. Postage, 7d. (Home).

4. Pre-excitation: A cardiac abnormality. Pathophysiological, patho-anatomical and clinical studies of an excitatory spread phenomenon bearing upon the problem of the W. P. W. (Wolff, Parkinson and White) electro-cardiogram and paroxysmal tachycardia. By R. F. Ohnell. 1944. Published by Henry Kimpton, London. Pp. 167. Illustrated. Price, 15s.

5. The migraine lesion: Describing the relief and cure of typical migraine by means of manipulative therapy. By H. Vincent Langley. Published by Research Books Limited, London. Pp. 26. Illustrated. Price, 6s. Obtainable from Messrs. William Heinemann (Medical Books) Limited, London.

6. Global epidemiology: A geography of disease and sanitation. By James Stevens Simmons *et al.* Volume I: Part I—India and the Far East. Part II—The Pacific Area. 1944. Published by Messrs. William Heinemann (Medical Books) Limited, London. Pp. xxvi plus 504. Illustrated. Price, 30s.

7. Venereal diseases and modern syphilotherapy. By K. D. Lahiri. Published by Himalaya Publications, Patna (Bihar). Pp. 193. Illustrated. Price, Rs. 2-15.

8. The diagnosis of nervous diseases. By Sir James P. Stewart. 1945. Published by Edward Arnold and Company, London. Price, 40s.

9. An experiment in the psychiatric treatment of promiscuous girls. By E. G. Lion *et al.* 1945. Published by Psychiatric Service, San Francisco City Clinic, City and Country of San Francisco Department of Public Health. Pp. 68.

Abstracts from Reports

ANNUAL REPORT OF THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION, MADRAS PROVINCIAL COUNCIL, 1944-45

This report in its introduction mentions the development of leprosy work planned as part of the post-war programme. 'The organization of an office of the Director of the Leprosy Campaign has brought leprosy into the forefront of the Government's post-war programme, and the year immediately after hostilities cease in the eastern theatre should show great advances in the development of the work in this province'. The report itself covers the following activities: Children's investigations unit at Saidapet; Rural unit at Madurantakam; Children's sanatorium, Ettapur, Salem District; Leprosy department, General Hospital, Madras; Urban leprosy unit and leprosy department, Stanley Hospital; Lady Willingdon leprosy sanatorium; work of the honorary publicity secretary; Field investigation; and Silver jubilee clinic, Madura.

It is impossible to comment in detail on the different sections of the report, but a few points which strike one may be mentioned. Epidemiological studies have shown that in a few areas the incidence in females appears to be higher than the incidence in males; there are usually special reasons for this; in most areas the incidence in males is considerably higher than the incidence in females, and also the disease tends to be more severe in males. Out of 249 cases in children observed with no treatment, 65 per cent showed improvement. Night segregation voluntarily enforced in certain villages over a period of several years is reported to have produced a fall in incidence of leprosy in these villages. The work of the Children's Leprosy Sanatorium is described; forty-nine children are in residence. In the Leprosy Department, General Hospital, Madras, patients under observation and treatment number about a thousand. In the Leprosy Investigation Centre at the Stanley Hospital, about 650 cases are under observation and treatment. Systematic annual examination of all school children for leprosy has been started, and 123 definite cases have so far been found among 17,738 children examined. The report on the work of the Lady Willingdon Leprosy Sanatorium, Chingleput, covers routine therapeutic investigation, special therapeutic investigation of new remedies, animal experimentation, immunological tests with lepromin, and studies of biopsy material. Drugs experimented with include iodized esters and oil (hydnocarpus), solupryidine cream, promanide ointment, dettol, and thiazamide for nasal lesions. Field investigations covered studies in leprosy in many villages, and the importance of marriage between different persons in different villages in the spread of leprosy from one village to another is stressed.

ANNUAL REPORT OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, FOR THE YEAR, 1944-45

In addition to the usual routine activities, research work was carried on a protozoal parasite of the central nervous system of animals suffering from rabies, which

might be concerned with the aetiology of rabies. The fact that the various stages of the parasite are regularly demonstrable in cultures of the brains of animals which died of natural or experimental rabies infection affords a simple and rapid method for the diagnosis of rabies in animals. In a case of recurring diarrhoea with severe epigastric pain, a large number of *Spirochaeta vincenti* (Blanchard) and *B. fusiformis* were noted in the faeces. Immediate relief was obtained by oral arsenicals, e.g. stovarsol and carbarsone, and complete cure by acetylarsan injections. This led to further investigation when Vincent's organisms were found in four persons with the same symptomatology, and *E. histolytica* and/or *Giardia intestinalis* in ten out of 120 persons whose faeces were examined. It is suggested in this report that cases of persistent diarrhoea with upper abdominal pain and emetine resistant cases of amoebic dysentery may be examined for fusospirochaetes in the faeces and, if found positive, treated with arsenical preparations.

Work in the Nutritional Research Laboratories included analysis of foodstuffs for vitamin, choline or fluorine contents, various animal experiments, and investigations on infantile beri-beri, lathyrism and other deficiency diseases. A course of lectures on nutrition were delivered to 26 Government officers.

The Southern India Branch of the Malaria Institute of India continued to work at the Institute during the year.

Correspondence

PHARMACY BILL

SIR,—May I suggest that opinions may be invited from teachers of materia medica and chemical examiners on the Pharmacy Bill which appears to have evoked a controversy in the lay press. Short notes limited to one-third of a column in small print will suffice. Four pages will give you opinions of twenty-four experts who use in the latest approved ways the pharmacist's stock.

S. D. S. GREVAL,

LIEUTENANT-COLONEL, I.M.S.

Imperial Serologist and Chemical Examiner
to the Government of India.

[Note.—Also see p. 39.

Will the medical men concerned and others who feel the urge kindly oblige.—EDITOR, I.M.G.]

PARENTERIC FEVER

SIR,—On page 567 of the *Indian Medical Gazette* for November 1945, in comment No. (2) on the term Parenteric Fever you state that 'Dorland's medical dictionary does not even mention enteric fever or the enteric group of fevers'. This comment is incorrect, for on page 449, second column of the medical dictionary quoted under Fevers, enteric fever appears and is defined as typhoid fever. Immediately following this entry appears 'Entericoid fever, any fever resembling typhoid in its clinical features'. This probably would be a better term to employ than parenteric fever to avoid confusion with the three known paratyphoid types, viz, 'A', 'B' and 'C'.

B. J. BOUCHE,

M.R.C.S., L.R.C.P.,

MAJOR, I.M.D. (Retd.).

'RULSTON MANOR',
BARLOWGANJ-MUSSOOREE, U. P.,
23rd February, 1946.

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL A. H. HARTY, C.I.E., Inspector-General of Civil Hospitals, C. P. and Berar, has been granted an extension of 5 days' leave and on its expiry he has been appointed as Surgeon-General with the Government of Bombay.

Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C., Chief Medical Officer and Inspector-General of Prisons in Baluchistan, is appointed to perform the duties of Civil Surgeon, Zhob/Loralai, in addition to his own duties, with effect from the forenoon of the 29th June, 1945, and until further orders.

The services of Lieutenant-Colonel W. H. Crichton, C.I.E., are placed at the disposal of the Government of the Central Provinces and Berar, with effect from the 20th August, 1945, for appointment as Director of Public Health, Central Provinces and Berar.

Lieutenant-Colonel B. K. Sheorey, Assistant Director-General (A.R.P.), is appointed additional Assistant Director-General, Indian Medical Service (Resettlement), with effect from the 1st September, 1945.

Lieutenant-Colonel E. T. N. Taylor, C.I.E., Additional Deputy Director, Indian Medical Service (Personnel), is appointed to carry on the current duties of the office of Deputy Director-General, Indian Medical Service in addition to his own, during the absence of Colonel A. K. Sahibzada, O.B.E., granted leave.

Major Jaswant Singh was appointed as Director, Malaria Institute of India, during the absence on deputation of Major-General Covell.

Major P. J. Wormald has been appointed temporarily as Assistant Director at the Central Research Institute, Kasauli, with effect from the 1st September, 1945.

Major M. N. Shah is appointed to be Additional Civil Surgeon, Delhi, with effect from the 4th October, 1945.

Captain D. H. Harrison is appointed to officiate as Civil Surgeon, Quetta/Sibi, with effect from the afternoon of the 30th June, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Major

A. Ahmad. Dated 20th June, 1945.

To be Captains

M. N. Bhan. Dated 8th February, 1944.

N. Bhattacharya. Dated 7th June, 1945.

T. G. Chandrasekhara Panikkar. Dated 14th June, 1945.

Jagdish Chandra Chugh. Dated 16th June, 1945.

Popuri Kaleswara Rao. Dated 20th August, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE (Special Emergency Commission)

To be Captain

J. W. A. Parsons. Dated 31st August, 1939.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Lieutenants

14th May, 1945

G. A. Pauljo.

E. F. Harbon.

C. B. J. Alexander.

R. S. Bewer.

A. Sen. Dated 13th June, 1945.

14th June, 1945

Bindiganavale Sreenivasiengar Narayanswamy.
Karingada Sebastian George.

15th June, 1945

Mulk Raj Katra. Dev Kumar Basu.
Bisheshwar Lal Agarwal. Dated 18th June, 1945.

19th June, 1945

Partap Bahadur Joshi. Suprabhat Banerji.

20th June, 1945

Nil Ratan Banerjee. Dharendra Narayan Roy.
Harbans Singh Gill. Dated 21st June, 1945.
Lionel George Pereira. Dated 2nd August, 1945.
Noshir Hormasji Antia. Dated 4th August, 1945.
Sanjiv Keshav Kudva. Dated 10th August, 1945.
A. G. Getting. Dated 10th August, 1945.
Ghulam Mohamed Salih Mohamed Soomro. Dated 16th August, 1945.
K. J. Vyas. Dated 17th August, 1945.

LEAVE

Major H. A. Ledgard, Civil Surgeon, Quetta/Sibi, is granted leave for 6 months, with effect from the afternoon of the 30th June, 1945.

Major G. Milne, Agency Surgeon, in Bundelkhand, is granted leave for 4 months, with effect from the afternoon of the 24th September, 1945.

PROMOTIONS

The undermentioned officer is granted the honorary rank of Colonel on reversion to pension establishment with effect from the date specified :—

J. J. H. Nelson, C.I.E., O.B.E., M.C., I.M.S. (Retd.). Dated 16th May, 1942.

Lieutenant-Colonel to be Colonel

G. R. McRobert, C.I.E. Dated 23rd August, 1945.

INDIAN MEDICAL SERVICE

Major to be Lieutenant-Colonel

G. F. Taylor. Dated 29th October, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS*(Emergency Commissions)**Captains to be Majors*

1st September, 1945

G. Das. D. R. Batura.
S. C. Chatterjee. B. C. Bhalla.
S. C. Mazumdar.

F. H. McCay. Dated 5th September, 1945.
N. A. Kuraishy. Dated 8th September, 1945.
G. B. Godbole. Dated 20th September, 1945.

23rd September, 1945

S. B. Sinha. H. N. Dastur.
A. Aziz. M. Sharma.
B. S. Sharma. P. N. Banerjee.
A. S. Baxi.

Lieutenants to be Captains

A. M. Kassim. Dated 31st August, 1945.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

*(Emergency Commission)**(WOMEN'S BRANCH)**Lieutenant to be Captain*

(Miss) J. B. Winstanley. Dated 22nd July, 1945.

RETIREMENT

Lieutenant-Colonel A. N. Bose, O.B.E. Dated 21st August, 1945.

RESIGNATION

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS*(Emergency Commission)*

Captain D. J. W. D'Costa. Dated 16th August, 1945, and is granted the honorary rank of Captain.

RELINQUISHMENTS

INDIAN MEDICAL SERVICE

(Emergency Commission)

Captain G. M. F. Dover relinquishes her Commission on account of ill health, 28th June, 1945, and is granted the honorary rank of Captain.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS*(Emergency Commissions)*

Captain P. J. Jhaveri, 23rd July, 1945, on grounds of ill health, and is granted the honorary rank of Captain.

The undermentioned officer is permitted to relinquish his commission on grounds of ill health, and is granted the honorary rank of Captain :—

Captain S. C. T. Arputhraj. Dated 2nd October, 1945.

Captain P. C. Shrinivasan, 20th October, 1945, on grounds of ill health, and is granted the honorary rank of Captain.

Captain Kunnariath Gopala Menon, 6th November, 1945, on grounds of ill health, and is granted the honorary rank of Captain.

Lieutenant A. S. Rao, 15th April, 1945, on grounds of ill health, and is granted the honorary rank of Lieutenant.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

The preparation of reprints entails rearranging the type, so that there is often a delay of a month or more, after the publication of the *Gazette*, before the reprints are ready. If reprints are not received within two months of publication of the *Gazette*, contributors should write to the Publishers.

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Original Articles

CAUSES OF HYPERGLYCÆMIA DURING OPERATION*

By P. DE, B.Sc., M.B. (Cal.), F.R.C.P. (Edin.), F.N.I.
Professor of Physiology, Medical College, Calcutta

and

S. DATTA, M.B.

Department of Physiology, Medical College, Calcutta

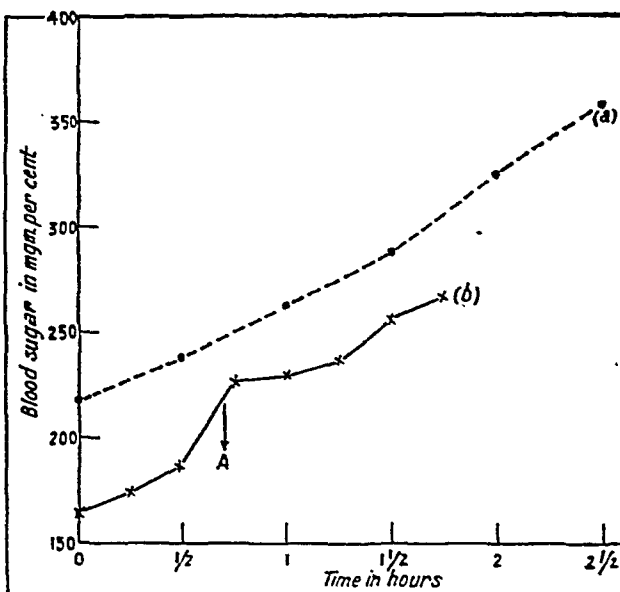
ADRENALINE hyperglycæmia is a physiological response at times of emergency. Blum (1901) was the first to note that adrenaline produces glucosuria. The immediate source of sugar of the blood is the liver glycogen.

A rise in blood sugar has been observed during surgical operations under anæsthesia. Cantarow and Gehret (1931) attributed the rise of the blood sugar level to the increased hepatic glycogenolysis, due either to the direct action of the anæsthetic used, or to increased hydrogen ion concentration associated with ether anæsthesia. Swan (1911) and Atkinson and Ets (1922) had shown that ether anæsthesia is always associated with hyperglycæmia in normal animals. Minnitt (1932) showed that a much greater hyperglycæmia was produced by ether than by nitrous oxide, and in a number of cases the blood sugar which was normal before anæsthesia rose to more than 200 mg. per cent after the operation. He showed that the blood sugar rose by variable but definite increments, and that it was much higher at the end of the operation than at the beginning; after the operation was finished there was a fall. He showed that in one of his cases the blood sugar was 178 mg. per cent after 5½ hours and 111 mg. per cent after 48 hours. He showed that the rise of blood sugar was irrespective of the method of anæsthesia, and obtained a rise of blood sugar with local and spinal anæsthesia as well. He concluded that the anæsthetic, or something associated with the operation if performed under a local anæsthetic, by stimulating adrenal bodies produced hypersecretion of adrenaline into the system. The production of hyperglycæmia by anæsthetics, whatever might be its cause, has been proved beyond doubt.

Now, the question is whether all the rise of blood sugar during operation can be accounted for by the anæsthetic used. This investigation has been undertaken with a view to ascertaining the exact cause or causes of the rise of blood sugar which is always found at the end of the operation. In order to study this matter it was considered desirable to use an anæsthetic which would give a uniform and steady result when given in accurate doses, and whose

effect would last for a fairly long time, at least till the experiments were over, because it has been shown by De (1946) that the rise of the blood sugar varies directly with the depth of anæsthesia. It was, therefore, decided to use urethane, 2 gm. per kilo body-weight of the animal, by the intramuscular route in every case except where otherwise stated. Cats were used in these experiments, and all operations were done three hours after the administration of urethane, when the animals were definitely anæsthetized.

Urethane anæsthesia produced a progressive and steady rise of blood sugar; a typical curve has been shown in graph I(a). The rise of blood sugar was, in every case, practically linear all through, except towards the end when the rise was more sharp in some of the cases. This rise, due to the anæsthesia, naturally complicated the determination of other possible factors, which also might be responsible for the rise of blood sugar. In order to determine the



Graph I.

(a)—Hyperglycæmia under urethane.

(b)—Urethane anæsthesia. Effect of operation on the blood sugar level.

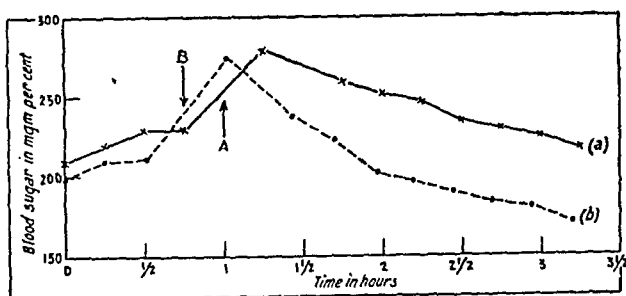
A—Period for operation. Note the rise in blood sugar level.

exact rôle of the operative interference on the blood sugar, it was, therefore, decided to perform two series of experiments which involved both simple and extensive operative interference. In the first series, three hours after the injection of urethane, samples of blood were drawn from the femoral vein of cats at 15-minute intervals, with the least possible operative interference, to determine the level of the rise of blood sugar during that period. These results, when plotted, indicated the level of the rise of blood sugar due to urethane only, and prolongation of this line practically indicated the level of the blood sugar at the particular moment. Then several operative measures

* Read at the Physiology Section of the 33rd Session of the Indian Science Congress held in January 1946.

such as opening the femoral vein, putting in the tracheal cannula, exposing the carotids, etc., were done in the same animal. The blood sugar of the sample taken immediately after the operation was observed to be always higher than the expected blood sugar at that time due to urethane anaesthesia only (*vide* graph Ib).

In the second series of experiments, preparations were made in which the steady rise of blood sugar normally seen under urethane was avoided. Anaesthetized cats were decerebrated at a low level in order to destroy the posterior hypothalamic nucleus, or decerebrated behind the level of this nucleus (De, 1946) or completely transected at the upper cervical region in order to produce hypoglycaemia after the operation. These procedures themselves involved a fairly extensive operative interference on the top of the anaesthetic used. It was noticed that though the blood sugar dropped after this operation, yet it did not come to the pre-operative level immediately. In all these experiments the blood sugar level was highest immediately after the operation, and it took about $1\frac{1}{2}$ to 2 hours to come back to the pre-operative level. Further, it was seen that the height of blood sugar noticed immediately after the operation was greater than the expected height at the time due to the anaesthetic only. The blood sugar level then steadily came down (*vide* graph IIa and b).



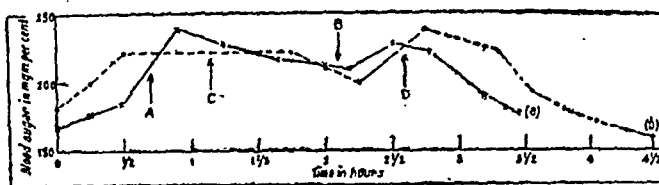
Graph II.

- (a)—Blood sugar level in spinal preparation done under urethane.
A—Period for operation. Note the rise of the blood sugar level.
(b)—Blood sugar level in decerebration at the colliculo-mamillary plane done under urethane.
B—Period for operation. Note the rise of blood sugar level.

In both these series of experiments, the 'excess' rise of blood sugar above the expected rise due to the anaesthetic must be attributed to factors other than the anaesthetic used. Can this 'excess' rise be due to the stimulation of the sympathetic and liberation of adrenaline?

Experiments were therefore performed in animals in which the sympathetic activity and the hyperglycaemic action of adrenaline were abolished with ergotoxine. In cats anaesthetized with urethane 10 mg. of ergotoxine were injected intravenously in repeated small doses. Such cats showed a fall of blood sugar after ergotoxine but when decerebration was done at

the colliculo-mamillary plane described by De (1946) on such ergotoxinized animals, a rise of blood sugar was still observed immediately after the decerebration, though this rise was less than that observed in similar experiments done without ergotoxine. This rise was followed by a steady and persistent fall (*vide* graph IIIb).



Graph III.

- (a)—Blood sugar level after spinal preparation.
A—Period for operation.
B—Left femoral vein opened and right axillary region dissected.
(b)—Blood sugar level after decerebration at the colliculo-mamillary plane in ergotoxinized cat under urethane.
C—10 mg. of ergotoxine injected in 75 minutes.
D—Period for decerebration.

The next question was to determine whether the peripheral nervous mechanism had any influence on the production of the hyperglycaemia due to operative interference. The spinal cord was transected at the level of the upper cervical region under chloroform and ether anaesthesia so as to remove the influence of the higher centres. In these animals operative measures, such as opening the femoral vein and dissection in the axillary region, after the effects of the previous operation of spinal transection had passed off, produced a transitory rise of blood sugar, after about 20 to 25 minutes. No rise of blood sugar was observed immediately after the operation (*vide* graph IIIa). A similar but more transient and smaller rise was produced in the ergotoxinized animals after similar operation following decerebration at the colliculo-mamillary plane.

Discussion.—A rise of blood sugar has always been observed after operations under general anaesthesia (De, 1946). The effects of fright, anxiety, emotional excitement, etc., before the anaesthesia, being so well known, have not been considered here. It has been shown in graph I(a) that urethane produces a steady rise of blood sugar, the rise being more or less linear in character throughout, except towards the end, when the rise is more sharp. So the 'excess' rise of blood sugar above that due to anaesthesia must be attributed to some cause or causes other than that of anaesthesia. It has been observed in experiments cited before (graph IIa and b) that any operative interference under general anaesthesia produces a greater rise of blood sugar than that due to anaesthesia alone. So the cause of this 'excess' rise must, therefore, be attributed either to the effect of the operation or to some other cause.

The operation itself stimulates the nerve endings at the site of the operation and supplies an impulse by which the centre is reflexly stimulated to liberate adrenaline which produces a high blood sugar. Also it has been observed that in ergotoxinized cats, decerebration produces a smaller rise of blood sugar immediately after the operation. It is known that ergotoxine inhibits the sympathetic activity and abolishes the hyperglycæmic action of adrenaline, and also it has been observed that ergotoxine produces a fall of blood sugar in urethanized cats. Therefore, the difference in the rise of blood sugar observed between these two experiments, done with and without the administration of ergotoxine, must be due to the stimulation of the sympathetic nerve endings at the site of the operation. Any rise that is noticed after ergotoxine cannot be due to reflex secretion of adrenaline, but must be due to a cause or causes other than anæsthesia or stimulation of sympathetics from the operative interference.

Now, the question resolves itself into one of finding out the cause of the rise of blood sugar noticed after the operation following ergotoxine. In experiments on spinal cats, it has been shown that any operative interference in these animals is followed by small transient rise of blood sugar which appears after a fairly long latent period (graph IIIa). A similar but smaller rise of blood sugar after a fairly long latent period has been observed in ergotoxinized cats when the same operations were performed, following decerebration at the colliculo-mamillary plane. This long latency precludes the possibility of its being reflex in origin, and favours the idea that it is possibly metabolic in nature. The high blood sugar that has been observed in Minnitt's case after $5\frac{1}{2}$ hours and 48 hours also suggests that it is due to metabolic disturbance.

It therefore appears clear that all the rise of blood sugar observed after operation should not be attributed to effects of the anæsthesia alone, but that the operative interference itself plays a fair part in it.

Summary.—The rise of blood sugar immediately after the operation is due to (a) the effect of the anæsthesia, (b) the stimulation of the sympathetic nerve endings due to the operative interference and (c) the metabolic activity.

We wish to express our most sincere thanks to Lieut. Colonel R. Linton, B.Sc., M.B., Ch.B., I.M.S., Principal, Medical College, Calcutta, for kindly providing us with all the facilities for doing this work. Also we express our best thanks to the members of the staff of this department for the ungrudging help that we have received from them in carrying out this investigation.

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PHENIODOL : A NEW DYE FOR CHOLECYSTOGRAPHY

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In the year 1924 Graham and Cole were able to visualize the gall-bladder for the first time by the intravenous injection of tetrabromophenolphthalein. Soon after this, iodine was substituted for bromine as the former has nearly twice the atomic weight of the latter. Later, the acid sodium salt of tetraiodophenolphthalein was found to be the best, and its oral administration for cholecystography has been the method of choice until very recently.

The results obtained with tetraiodophenolphthalein show a very high degree of accuracy. Unfortunately, this dye produces unpleasant symptoms in some patients, and since 90 per cent of the dye is eliminated by the gastrointestinal tract it very often obscures the gall-bladder by its presence in the hepatic flexure. Some patients get severe diarrhoea which is accompanied by the production of wind in the large gut which further obscures the gall-bladder. Great patience and perseverance is required to get rid of the dye and the wind in the hepatic flexure. All these difficulties are often very annoying and tiring both to the radiologist and the patient.

In 1940 Dohrn and Diedrich working in the laboratory of Schering A. G., Berlin, discovered a new dye—a-phenyl-(4-hydroxy-3:5-di-iodophenyl) propionic acid—which has surmounted most of the difficulties met with the phenolphthalein compound. The Germans called it 'Biliselectan.' As soon as papers giving information about this compound reached the allied countries, experiments were made and details perfected in the manufacture of this compound. The Medical Research Council gave it the official name of 'Pheniodol.' In the United States of America it has been named 'Priodax.' It is a white odourless powder, soluble in alkali, ether, alcohol and acetone, but insoluble in water. It is very bitter to the taste, but this bitter taste can be masked. It is sold as pheniodol powder, pheniodol meal and pheniodol sugar-coated granules, and in U.S.A. as priodax tablets. This dye is given by the oral route only. Most of it is excreted by the kidneys.

I have used this dye in 35 patients. Only four patients complained of a bitter burning taste and this also only on interrogation. Two patients vomited after pheniodol. Both were very weak and emaciated. Sixteen patients showed a very mild diarrhoea usually with a

single large motion. Only two patients complained of marked diarrhoea. One of these two patients had, on a previous occasion, been given the old phenolphthalein compound, and had developed severe diarrhoea and vomiting. With the new dye, the diarrhoea was less severe, and there was no vomiting. None of the patients showed the dye in the colon, and of the patients who were given a subcutaneous injection of $\frac{1}{2}$ c.cm. of pitressin, none showed gas in the hepatic flexure. Nine patients complained of a burning sensation in the urethra on micturition: in two cases it was very severe. This symptom disappeared after the second or the third micturition.

Comment

The new gall-bladder dye is, in my opinion, a great improvement on the phenolphthalein compound.

The difficulties with the phenolphthalein compound are not insurmountable, but the new medium gives far less trouble.

The contra-indications are the same as with any iodine compound.

Pheniodol is sold as sugar-coated granules and as pheniodol meal. In both the bitter taste is masked. The results with both are similar but the sugar-coated granules produce less or no burning in the mouth or throat provided the patient does not chew or suck them.

A single dose equivalent to three grammes of pheniodol gives very good results in an average case. In patients weighing more than 14 stones, we have very safely given $4\frac{1}{2}$ to 6 grammes equivalent of pheniodol. The method of preparation for the patient is the same as with the old medium.

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FURTHER CASES OF INTEREST SEEN AT THE WILSON RADIOLOGICAL DEPARTMENT OF THE ERSKINE HOSPITAL, MADURA*

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(A) Digestive system

Case 1.—Broncho-oesophageal fistula (see figure 1, plate V). A male, aged 25, complaining of dysphagia. Stricture of the oesophagus

was suspected. Under fluoroscopy, on 7th December, 1944, a spoonful of barium-swallow made him cough, and the emulsion was forced into the left bronchus. The skiagram shows the fistula; and the irregularity of the lumen of the oesophagus is suggestive of malignancy.

Case 2.—Diverticulum of the stomach (see figure 2, plate V). A male, aged 30 years, admitted for investigation of dyspepsia. Barium meal examination on 3rd December, 1945, revealed a gastric diverticulum, in which barium persisted after the stomach had emptied.

Case 3.—Rotation of the duodenal cap in peptic ulcer (see figure 3, plate V). A female, aged 48 years, with symptoms of peptic ulcer. X-ray examination on 1st March, 1943, showed rotation of the duodenal cap to the left, which is considered to be pathognomonic of an infiltrated ulcer. Laparotomy showed the first part of the duodenum dislocated, and the liver and pancreas adherent; there was obstruction to the stomach contents, and a suggestion of malignancy.

Case 4.—Peri-cholecystitic adhesions (see figure 4, plate V). A female, aged 46 years. Barium meal examination on 3rd March, 1943, showed a lateral angling of the Pars descendans duodeni, possibly due to adhesions between the duodenum and the gall-bladder. No operation was done here.

Case 5.—Small bowel obstruction (see figure 5, plate V). A female, aged 30 years. The radiograph (29th July, 1941) shows well-marked distension and a concertina-like appearance of the small bowel, due to obstruction.

Case 5a.—Jejunal stasis (see figure 5a, plate V). A male, aged 35 years, was radiographed on 13th September, 1943, for the investigation of a tumour in the left hypochondrium of seven months' duration. The jejunum, throughout, showed a fixed pattern-ness, which is seen in the skiagram, persisting at six hours after the barium meal administration, when practically the rest of the meal is in the colon. This would seem to be either a case of jejunitis (of which we have had several examples here), or one of those very rare instances of jejunal carcinoma. Clinically, a nodular mass was felt in the left hypochondrium.

Case 6.—Tuberculosis of the caecum (see figure 6, plate VI). A female, aged 30 years, x-rayed on 5th March, 1943. The typical Stierlen's sign (barium filling of the terminal ileum and hepatic flexure, and a gap in-between) was present. This sign, though not pathognomonic of tuberculosis, is none the less a valuable diagnostic finding.

Case 7.—Tumour abdomen (see figure 7, plate VI). A male, aged 40 years, with symptoms suggestive of carcinoma of the hepatic flexure, or chronic intussusception. The skiagram taken on 16th October, 1945, shows a filling defect of the proximal portion of the transverse colon; and a radiological diagnosis.

* Supplementary to the article in the *Indian Medical Gazette*, Vol. LXXVIII, of July 1943.

of an extrinsic tumour causing pressure deformity was suggested. Laparotomy revealed a glandular tumour outside the lumen of the bowel, which was intact.

Case 8.—Intestinal polyposis (see figure 8, plate VI). A male, aged 56 years, with a history of passing blood and mucus per bowel, since 3 weeks.

A barium enema examination on 20th September, 1943, showed a beehive appearance of the descending colon in its middle two-fourths. A previous barium meal examination revealed a hold-up at the splenic flexure. While malignancy cannot be ruled out, the appearances are suggestive of polyposis.

(B) Respiratory system

Case 9.—Bronchogenic carcinoma (see figure 9, plate VI). A male, aged 45 years. Plain x-ray of the chest showed a kidney-shaped shadow in left hilar zone, associated with effusion in the left pleural cavity, and was suggestive of a carcinoma. Bronchography with iodized oil on 1st October, 1945, showed broncho-stenosis of a main branch of the left bronchus.

Case 10.—Bilateral hydatid cyst (see figure 10, plate VI). A child, aged 6 years, with a nodular swelling below xiphisternum, and enlarged liver, associated with fever, and pain in the abdomen of 5 days' duration suggestive of a tumour in the hypochondrium. The skiagram taken on 16th July, 1945, showed a cystic tumour in either lung. There was a third one in the liver.

Case 11.—Congenital cystic disease of the lung (see figure 11, plate VI). A male, aged 23 years. Intratracheal injection of iodized oil and x-ray on 27th July, 1944, revealed a condition of cystic disease of the lung.

(C) Circulatory system

Case 12.—Patent inter-auricular septum (see figure 12, plate VII). A boy, aged 15 years, with congenital heart; there was breathlessness associated with cyanosis, but no clubbing was present. X-ray examination on 19th March, 1945, showed a patent foramen ovale as the main defect, the enlarged right hilum clinching the diagnosis.

Case 13.—Pericardial effusion (see figure 13, plate VII). A boy, aged 12 years. Examined on 26th February, 1945. The typical 'tobacco pouch' heart is seen. About 12 oz. of fluid were aspirated.

(D) Skeletal system

Case 14.—An unusual type of fracture of cervical spine (see figure 14, plate VII). A female, aged 39 years, admitted with quadriplegia, consequent on a fall. Bed x-ray taken on 19th September, 1944, shows an unusual type of fracture, the bodies of the 3rd, 4th and 5th cervical vertebrae being involved (a true lateral view was not found feasible).

Case 15.—Scurvy (see figure 15, plate VII). A child, aged 2 years. X-rayed on 11th August, 1945, for suspected osteomyelitis of femur. Radiographs show the typical splaying and condensation of the lower end of the femoral diaphysis, and raising of the periosteum due to sub-periosteal hæmorrhage. Treatment with vitamin C preparations brought about a cure.

Case 16.—Post smallpox joints (see figure 16, plate VII). A female child, aged 10 years, was x-rayed on 16th January, 1943, for deformity of both elbows and left wrist. There was a previous history of smallpox. The destructive changes about the epiphyses in the left wrist and elbow are well marked.

Case 17.—Osteochondromatosis (see figure 17, plate VII). A female, aged 48 years, was complaining of pain in the knee. The skiagrams taken on 29th July, 1944, show the presence of several loose bodies.

Case 18.—Marie-Strümpell type of arthritis (see figure 18, plate VII). A male, aged 30 years, was having pain and rigidity of the spine. X-ray examination on 19th November, 1943, shows the typical 'bamboo-spine', with ossification of several ligaments.

(E) Miscellaneous

Case 19.—A female, aged 25 years (see figures 19 and 19a, plate VIII), was admitted on 14th March, 1943, for gun-shot wounds in the abdomen. The skiagrams show her abdomen sprayed with shots, both in and outside. While in hospital, she showed no rigidity of the abdominal wall, and scarcely ran a temperature. Two of the shots were removed from her anterior abdominal wall, and ten were passed out per rectum. She was discharged cured on 17th May, 1943; and, when seen several months afterwards, looked quite fit.

Case 20.—Congenital malformation (see figure 20, plate VIII). A male child, aged 2 years, x-rayed on 16th December, 1944. The picture shows multiple hemivertebrae, fusion of the ribs, spina-bifida of the lumbo-sacral region, etc., associated with spinal scoliosis. The nature of the extraordinary bone-segments, seen on either side of the lower lumbar spine, is not clear.

My sincere thanks are due to Lieut.-Colonel A. S. Leslie, I.M.S., Superintendent of this hospital for his courtesy, and kindness in permitting me to make use of the hospital records.

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A CLINICAL STUDY OF TWENTY CASES OF NEURO-CIRCULATORY ASTHENIA IN CIVILIAN PRACTICE

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Introduction

NEURO-CIRCULATORY ASTHENIA (NCA) also known as effort syndrome, disordered action of the heart, the irritable heart of soldiers, and as DaCosta's syndrome, is a condition of abnormal functional irritability and instability of the nervous and circulatory systems. The American terminology, neuro-circulatory asthenia, is to be preferred, since it lays emphasis on the neurasthenic as well as the circulatory symptoms which form the chief clinical features of the disorder.

Though more common in soldiers during war time, the syndrome is not rare in civilians. Extreme physical effort may bring about symptoms of circulatory distress such as dyspnoea, palpitation, præcordial pain, weakness, dizziness, faintness and tremor. Further effort is prevented by the earlier onset of fatigue of the neuro-muscular apparatus. Since this group of symptoms is brought about by effort, it has been called effort syndrome. The effort syndrome is more easily brought about in the weakly, physically ill-trained, sick, tired, or nervous subject. In the normal well-trained subject the first symptom to limit further activity is dyspnoea. In poorly built, weakly nervous subjects, these symptoms may become manifest merely on excitement with little or no effort, palpitation and not dyspnoea being the presenting feature. The recognition of this distressing functional disorder is of the greatest importance, since organic heart disease must be excluded before proper treatment can be instituted.

Ætiology

Age.—The age incidence in my series of 20 cases was between 20 and 25 years in the majority of the cases. The youngest was 18 and the oldest 32 years.

Sex.—Eighteen males and 2 females were affected. This incidence seems to show that the male is more commonly affected.

Heredity.—Often one of the parents at least is highly strung and nervous.

Strain.—Financial or family worries, emotional conflicts, nervous or physical fatigue, debility from infections may all be contributory causes. Though tea, coffee and tobacco do not by themselves give rise to neuro-circulatory asthenia, there is no doubt that they are made worse by their use.

Social status.—All my patients were fairly well educated and intelligent. The country folk seem to be rarely affected.

Nutrition.—Though the well-nourished subject is not exempt from the condition, the disorder seems to be especially common in the under-nourished. In most of my cases the subject was lean, lanky, under-nourished and rarely inclined to play games.

The cause of the abnormal irritability and undue fatigability of the central nervous system has not yet been explained. Why cerebral symptoms are dominant in some and gastro-intestinal or cardiovascular in others is also unknown. All that can be said is that neuro-circulatory asthenia seems to occur in certain subjects who seem to be constitutionally inferior and endowed with a hypersensitive nervous system, on account of which they find themselves unable to withstand the stresses and strains of modern life. In his Goulstonian lectures, Wood (1941) has adduced evidence to show that the syndrome is the manifestation of emotional stimulation, usually fear. It should therefore be regarded as a psychoneurosis giving rise to somatic phenomena which may be cardiac, respiratory or gastro-intestinal depending upon the different reactive patterns to psychological distress; and so it really comes within the realm of the psychiatrist. Many attempts have been made to explain the somatic disorder by the altered biochemistry of blood. There is no evidence of decreased oxygen tension in the blood. The circulation time also is within normal limits. Soley and Shock (1938) came to the conclusion that the alkalosis resulting from hyperventilation produces the symptoms. The investigations of Guttman and Jones (1940) do not support this view. Hyperventilation was not a presenting feature in my cases; it was really a rapid shallow breathing and not a true hyperpnoea which washes out the carbon dioxide to produce alkalosis. Moreover, palpitation, which is extremely common in neuro-circulatory asthenia, does not seem to be a manifestation of the hyperventilation syndrome. From their investigations on the effect of exercise on soldiers with effort intolerance, Jones and Scarisbrick (1943) concluded that fatigue was not a result of respiratory alkalosis, though the bicarbonate content may become slightly lowered subsequent to the production of lactic acid. In their experiments, the lactic acid showed a response similar to normal persons. The average man becomes exhausted when the lactic acid content of the blood is about 100 mg. per 100 c.cm. In effort syndrome, it was found that most of them desisted from work when the lactate level was still quite low. From these facts it becomes clear that the patient's physiological response to exercise is not different from that of the normal subject, though he stops work earlier than the normal subject. In other words, it is reasonable to conclude that a psychological and not physiological abnormality is the cause of asthenia.

Symptoms

The chief manifestations are fatigue (90 per cent), nervousness (75 per cent), palpitation (95 per cent), dizziness (60 per cent), fainting (15 per cent), headache (40 per cent), breathlessness (90 per cent), hyperidrosis (75 per cent), tremor (60 per cent), precordial pain (75 per cent), xerostomia (20 per cent), insomnia (30 per cent), anorexia (25 per cent), frequent micturition (20 per cent), and unexplained phobias (20 per cent). These symptoms are usually brought about by effort or excitement in young hypersensitive nervous subjects, and in bad cases they may become manifest with little or no provocation. They are made worse by nervous strain and infection.

Signs

The physical build is often poor, the chest being long and narrow. A nervous manner is easily observed. Tachycardia is the rule. The pulse rate which ranges between 90 and 100 per minute at rest may even go up to 120 or 130 on slight provocation. The sleeping pulse rate is within normal limits (65 to 75). The hands are cold and moist with sweat, and this hyperidrosis is sometimes very distressing. Visible axillary sweating is not uncommon. Overaction of the great vessels may be evident at first sight. Tremor is common. The knee jerks are very brisk.

Cardiovascular system.—The apex beat is normally situated. It may be forcible, and there may be a wavy impulse over the precordium. A systolic murmur is not uncommon, but it does not possess the usual characteristics attributed to organic murmurs. Apart from overaction of the heart, there is no evidence of any organic disease.

Blood pressure.—The systolic blood pressure is higher than the normal average and it is often very labile. I have seen the blood pressure going up to 160 and coming down to 130 in a few minutes. It may rise quickly from 120 to 160 with little or no cause. The diastolic pressure is not much elevated. The cold-pressor test which was done in ten cases revealed an average rise of 18 units of mercury for the systolic and 8 units for the diastolic pressure.

Fundus oculi.—On ophthalmoscopic examination, there may be visible pulsation of the vessels. The arteries were visibly pulsatile in 5 cases.

Electrocardiogram.—The electrocardiogram was normal in most of the cases. The only abnormalities detected were as follows :

- (1) Low voltage in lead I—3 cases.
- (2) Slurring of R wave in lead I—2 cases.
- (3) Inversion of T wave in lead II—2 cases.
- (4) Inversion of T wave in lead III—4 cases.
- (5) Right axis deviation—3 cases.

Apart from these changes, there were no other abnormalities except tachycardia (90 to 120 per minute). The abnormalities detected

do not seem to indicate any organic cardiac lesion. Low voltage in lead I is by itself of no consequence. Slurring of the R wave in lead I was associated with a low voltage ; therefore, it cannot be considered as indicative of damage. The inversion of T wave in lead II was not associated with any significant changes in the Q wave. Inversion of T wave in lead II has been observed in excited subjects before anaesthesia. Inversion of T wave in lead III is often physiological. Right axis deviation seems to have been a manifestation of a vertically disposed heart ; for on radiological examination the appearance of the heart was that of the 'dropped' type.

Electrocardiograms taken in five cases after exercise did not reveal any changes suggestive of insufficient coronary circulation. Apart from tachycardia, there was no other abnormality as compared with the electrocardiogram taken before exercise.

Vital capacity and B.M.R.—The vital capacity was measured in ten cases. It was found to be diminished as a rule. The average was 2,200 c.cm. The B.M.R. (Benedict-Roth apparatus) was carried out in five cases and found to be within normal limits in all of them. It is very difficult to measure the B.M.R. in these patients, since their breathing is extremely irregular and the tracings obtained practically useless for interpretation. A tendency to sighing respirations is also common. The ability to hold the breath is impaired, many of the patients being unable to hold their breath for even 10 seconds.

Blood.—The hæmoglobin, red cell count, erythrocyte sedimentation rate, fasting blood sugar and glucose tolerance tests were within normal limits. The W.R. was negative in all cases.

Urinary findings.—The only abnormal urinary findings were benign albuminuria (three cases) and oxaluria (four cases). Transient glycosuria was observed in two cases. The efficiency of the kidneys as judged from concentration tests in eight cases was normal.

X-ray examination was done as a routine in all cases. In no case was the heart enlarged. In fact, the heart often looked smaller than normal and sometimes vertically disposed. The overaction of the heart was easily observed on screening.

Differential diagnosis.—Neuro-circulatory asthenia is often confused with organic heart disease, thyrotoxicosis and pulmonary tuberculosis. In organic heart disease the type of the murmur is different and cardiac enlargement may be demonstrable. Electrocardiography and x-ray examination may give valuable information. In case of doubt it is best to watch the patient for a few months before diagnosing organic heart disease. In thyrotoxicosis, patients often deny that they are ill and are eager to go back to work ; their manner is alert and aggressive ; their hands are warm and moist and the

sleeping pulse rate and B.M.R. are both increased. On the other hand, in neuro-circulatory asthenia the patients have numerous complaints and welcome restriction of their activities; their attitude suggests despondency and inactivity; their hands are cold and moist and the sleeping pulse rate and B.M.R. are normal. Pulmonary tuberculosis must be ruled out after a careful examination of the lungs, including radioscopy.

Course and prognosis

The course of neuro-circulatory asthenia is very variable. There are several grades in the severity of the condition. Though complete recovery is possible there is always a probability of recurrence after infection, worry and emotional stress. Neuro-circulatory asthenia does not cut short life though it may cause the patients to lead crippled lives. There is no evidence that neuro-circulatory asthenia is a precursor of organic heart disease.

Some of my patients have been watched for more than four years, and there is no evidence of hypertension having supervened in any of them.

Treatment

It is essential to reassure the patient and win his confidence by dispelling all his fears of cardiac disease. The cause of the malady should be explained to him. A thorough examination of the patient including electrocardiography and radiography should be done. It is unwise to start treating these patients with drugs. They seem to be particularly sensitive to digitalis and strychnine. Digitalis increases the irritability of the heart; tonics containing strychnine increase the irritability of the nervous system. To allay nervousness, sedatives like bromides and luminal may be helpful. Some cases are best dealt with by a competent psychiatrist. There is no doubt that in many cases the syndrome should be considered as a neuro-psychiatric and not a cardiovascular problem.

Attempts have been made to cure the condition by surgical treatment such as denervation of the adrenals (Crile, 1934). There is no doubt that emotions increase adrenalin secretion, and many of the symptoms may be due to it. An injection of $\frac{1}{2}$ c.cm. of adrenalin to these patients brings on the symptoms of neuro-circulatory asthenia. But denervation of the adrenals is a serious operation. It is much easier to irradiate the adrenals. At the suggestion of Dr. A. C. Devaraj, Radiologist of the Krishnarajendra Hospital, five of the fairly severe cases were subjected to irradiation. All of them improved. One had a mild relapse after a year. It may be necessary to irradiate again such a case. This method of treatment is simple and worth a trial. Further observation is necessary before assessing its full value.

The general management of these cases is of the greatest importance. They must attune

their lives to a low key and avoid emotional upsets and excess of tobacco, coffee and tea.

A daily injection of 5 to 10 units of insulin (with glucose by mouth) for 6 to 8 weeks increases the appetite and helps to improve their physical build. Five of my patients improved by this line of treatment. Insulin should be cautiously given since some of them are sensitive to it. Sodium chloride and eucortone, which are so useful in the treatment of the myasthenia of Addison's disease, do not seem to be of much value in neuro-circulatory asthenia.

Summary

A study of twenty cases of neuro-circulatory asthenia is given. It is not a rare condition in civilian practice. The symptoms, differential diagnosis and treatment are briefly discussed. The cause of the undue excitability and fatigability of the neuro-muscular apparatus is not known. There is no evidence of any altered physiology in these patients. The clinical, radiological and laboratory findings are suggestive neither of the presence nor of the subsequent supervention of any organic lesion. In many cases it is better to consider the syndrome as a neuro-psychiatric rather than as a cardiovascular problem. Irradiation of the adrenals is a simple procedure worth trying in these cases.

Acknowledgments

I would like to record here my thanks to Rajavaidya Pravina Dr. C. Krishnaswami Rau for the facilities given to me; to the staff and technical assistants of the Sri Krishnarajendra Hospital for their co-operation; and to Dr. Srikantia for kind criticism and encouragement I received in the preparation of this paper.

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SOMATIC TÆNIASIS (SOLIUM CYSTICERCOSIS)*.

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 Madras

SEVERAL cases of somatic tæniasis have been reported in India as well as among British

* Paper rearranged by the editor.



Fig. 1.



Fig. 2.



Fig. 3.



Fig. 5.

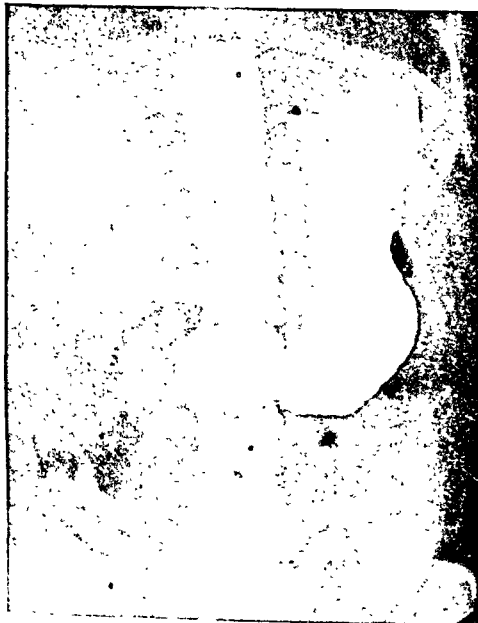


Fig. 4.



Fig. 5a.



Fig. 6.



Fig. 7.



Fig. 8.



Fig. 9.



Fig. 10.

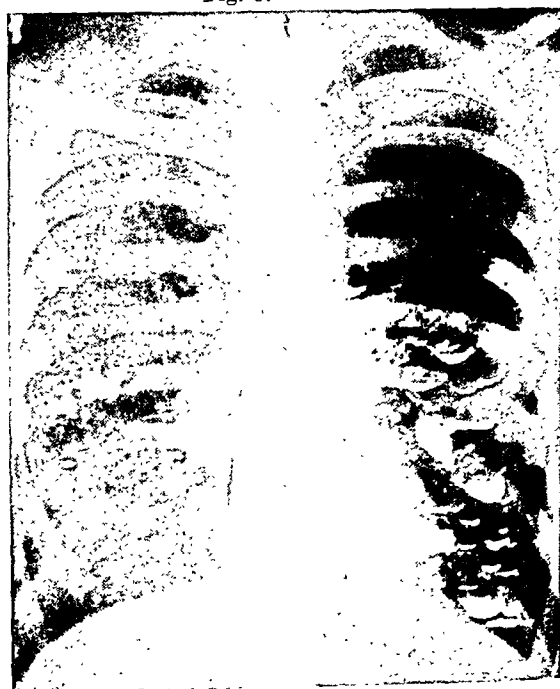


Fig. 11.

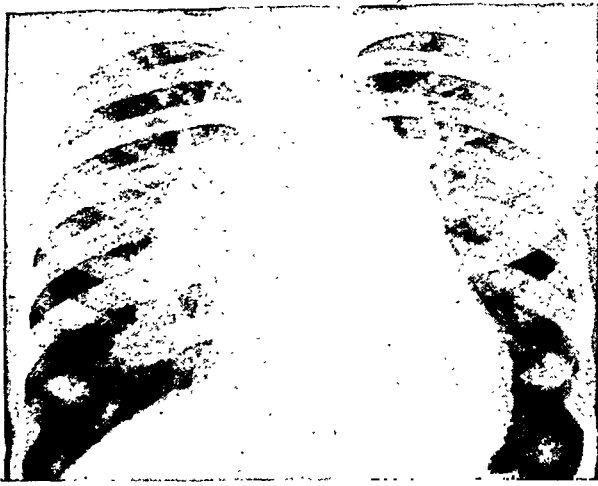


Fig. 12.



Fig. 13.

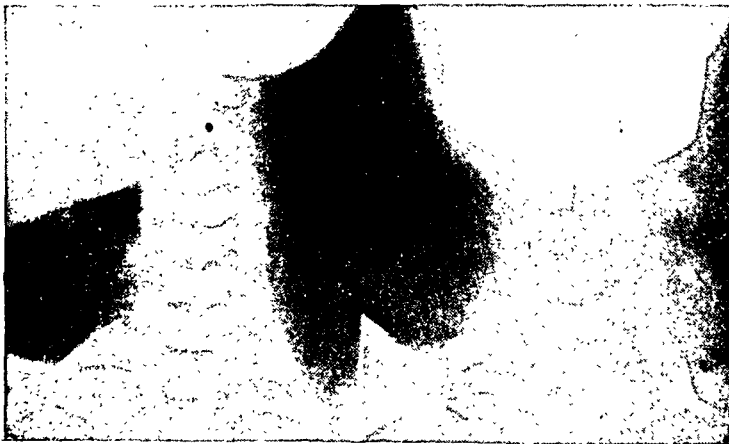


Fig. 14.



Fig. 15.

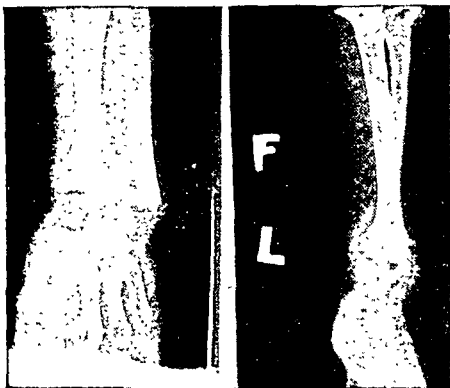


Fig. 16.

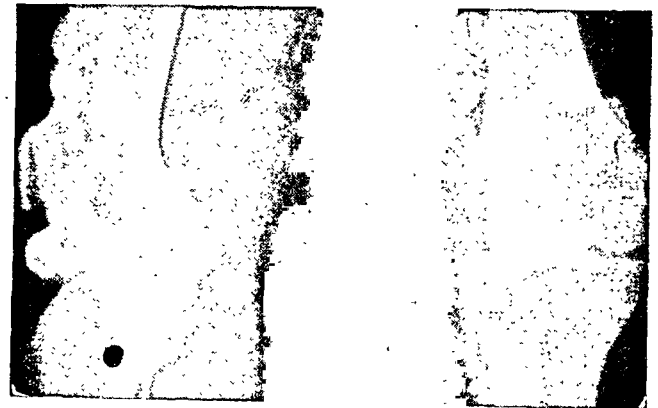


Fig. 17.



Fig. 18.



Fig. 19.



Fig. 19a.

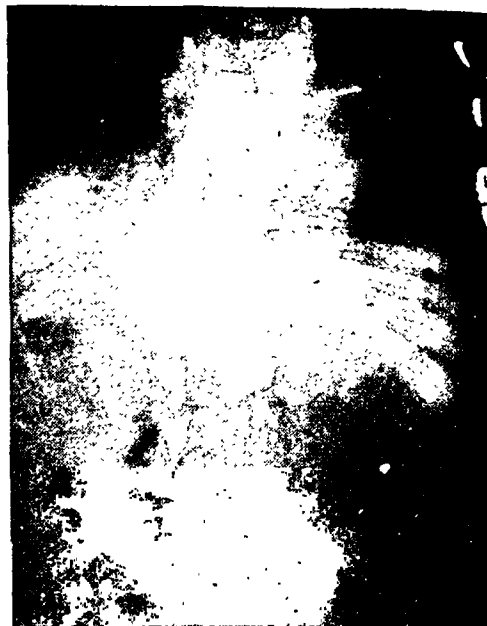


Fig. 20.

SOMATIC TÆNIASIS (*SOLIUM CYSTICERCOSIS*) : R. SUBRAMANIAM. PAGE 64.



Fig. 1.—Showing muscular build of the patient.



Fig. 2.—Section of cyst. Low power.

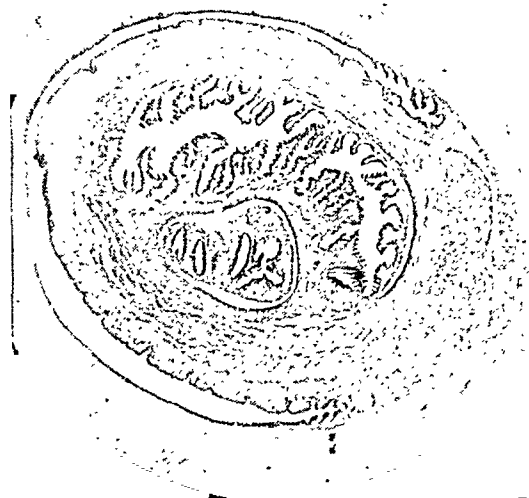


Fig. 3.—Section of cyst. High power.

soldiers returning from India. McRobert (1944) reported a case of somatic tæniasis and stated that diagnosis can usually be made on x-ray examination, by visualization of the partially calcified cysticerci. In the available literature frank epileptic fits have been reported but no other epileptic manifestations. The following case in which fugue* was a prominent symptom will therefore be of interest.

The patient, a Hindu male, aged 20 years, was admitted on 25th September, 1945, with inability to attend to himself since six months. He was a non-vegetarian taking pork and beef, and accustomed to alcohol (toddy and brandy). His brother, who accompanied him, looked rather thinly built, like an emaciated Indian peasant, but the patient looked apparently a very robust person with a well-developed 'wrestler's' body (figure 1, plate VIII).

The history given was a gradual onset of lethargy; the patient was found to be doing things at a much slower rate than before, and later he was doing no work but would sit down wherever he was. He did not attempt to clean himself, and he passed urine and stools in the bed. The appetite was good. He had a tendency to wander about without any object; he fell from a height in one of his wanderings, fracturing his second lumbar vertebra, and had to be put in a plaster case. His intelligence and behaviour were below normal, and he answered questions in a hesitant manner.

A number of 'blubbery' nodules were felt under the skin, practically all over the body. The cysts were more in evidence in the neck, arms, thighs and back, varying in size from that of a pea to that of a small marble. The central nervous, cardiovascular, respiratory, and alimentary systems were normal. Fundus examination was also normal.

The urine and stool examinations gave normal findings. The total white cell count was 6,200; the differential count was: polymorphs 61 per cent, lymphocytes 24 per cent, eosinophils 14 per cent, and monocytes 1 per cent. The x-ray picture of the skull and back was normal, and no calcified cysticerci were visualized. The biopsy of a nodule, however, showed the presence of *Cysticercus cellulosea* (figures 2 and 3, plate VIII).

This case presents some features in common with the case reported by McRobert. The patient showed the 'professional wrestler' type of body; the diagnosis was made before the cysticerci were calcified; there was a fairly high count of eosinophils (14 per cent). So far no satisfactory treatment has been evolved for this condition.

My thanks are due to the Superintendent and other members of the staff of the Government General Hospital for their kind help.

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* 'Fugue' is defined as a disturbance of consciousness in which the patient performs purposeful acts, but after the state has passed he has no conscious remembrance of his actions during the period. This report does not clearly indicate whether this was so in this case.—*Editor, I.M.G.*

MULTIPLE DEFICIENCY FOLLOWING DIET RESTRICTED FOR DIARRHOEA

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and

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A BENGALI female, aged 30 years, was admitted to this hospital on 13th December, 1945, with diarrhoea, spasmodic abdominal pain, sore mouth, swelling of the legs and a hæmorrhagic rash on both extremities. The diarrhoea started eight months ago when she was eight months pregnant, and for this diarrhoea her diet was gradually but drastically reduced, so that for about two months before admission she had had practically nothing but barley water. It was during these two months that the other symptoms developed, at first sore mouth, then oedema, and lastly the rash which was only of fifteen days' duration.

On admission, her general condition was poor; she was emaciated, with oedema of the legs, glossitis, angular stomatitis, thickened colon and a hæmorrhagic rash on both extremities in the form of petechæ and echymoses (figure 1, plate IX). No other abnormality was detected.

Laboratory investigations: White cell count 8,000 per c.mm., with polymorphs 60 per cent, lymphocytes 16 per cent, large mononuclears 3 per cent, and eosinophils 11 per cent. Red cells 3.70 millions, macrocytosis (MCV 110.8 μ); platelets 296,000 per c.mm. van den Bergh test negative; no parasites seen. Total serum protein (copper sulphate method) 3.75 grammes with albumin fraction (biuret method) 1.43 grammes, and globulin 2.32 grammes per 100 c.cm. W.R. negative. Gastric analysis showed absolute achlorhydria. The urine was clear. The stools were loose and pale, but showed no pathogenic organisms on repeated examinations, the total fat content being 30 per cent of the dried weight. The vitamin C excretion in urine was 3.5 mg. in 24 hours.

Barium meal examination: The picture of the stomach suggests gastritis, a residue at five hours. As regards the small intestine, the distribution in the early stages is unusual. In the jejunum the opaque meal is collected into 'clumps' (figure 2, plate IX, three hours after taking the meal) indicating poor peristalsis. There are no fluid levels however. There is a large residue in the terminal coils at seven hours, indicating ileal stasis, while the transverse colon is grossly irregular (figure 3, plate IX).

Diagnosis.—This was a case of malnutrition suggestive of the sprue syndrome with obvious clinical manifestations of ariboflavinosis, scurvy, and hypoproteinaemia. The peculiarity of her scurvy was the extensive hæmorrhagic rash scattered on the extremities, with no bleeding gums.

Treatment.—She was put on a mixed diet which controlled her diarrhoea within a week. The diet was supplemented by injections of vitamin C 200 mg. daily for seven days, and proteolysed liver extract (the equivalent to 100 gm. of raw liver being given daily) by mouth for ten days. This further improved her condition, the rash cleared up completely, there were no fresh hæmorrhages, but her mouth was still very sore. She was given riboflavin 6 mg.

a day for about a week; this relieved the soreness although the tongue was still smooth and reddish. In spite of this improvement it was noticed that her red cell count was stationary at 3.8 millions and that the size of the cells and the hæmoglobin were decreasing; she was therefore put on iron, and in a week's time the red cell count went up to 4.4 millions and hæmoglobin to 90 per cent.

Discussion.—The patient had originally diarrhoea, which persisted, probably because of severe restriction of diet, especially at a time when there was an extra physiological demand. In any case, it gave rise to various deficiencies. She had absolute achlorhydria, ariboflavinosis, vitamin-C deficiency, a dimorphic type of anæmia, and also hypoproteinæmia and œdema. The x-ray pictures of the intestines appear to be of the 'deficiency pattern'; another barium meal series taken during convalescence showed a more normal appearance of the small intestine at three hours (figure 4, plate IX), and a barium enema (figure 5, plate IX) showed a fairly normal appearance of the transverse colon.

The treatment of diarrhoeas with severe restriction of diet for a long period appears to be still too common in our country; it not only prolongs the duration of the disease but also adds complications to it.

EXPLANATION OF PLATE IX.

Fig. 1.—Photograph of the patient showing hæmorrhagic rash.

Fig. 2.—Small intestines. Three hours after barium meal.

Fig. 3.—Small intestine and transverse colon. Seven hours after barium meal.

Fig. 4.—Small intestine after treatment. Three hours after barium meal.

Fig. 5.—Large intestine. After barium enema.

PULMONARY AMŒBIASIS

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AMŒBIASIS of the lung is much more frequent than is usually thought, but it often remains undetected, or perhaps is wrongly diagnosed as pulmonary tuberculosis. Clinical recognition of the condition is rarely reported, while the radiological findings, if present, are apt to be missed or misinterpreted. Dormer and Friedlander (1941) reported seven cases, all responding to emetine. The symptoms present were cough, hæmoptysis, loss of weight, night sweats and evening rise of temperature—in fact, all symptoms highly suggestive of pulmonary tuberculosis. Mencía (1944) reported a case of bronchial amœbiasis in a girl who was listless for a period of seven months and

then developed a cough. Gradually she began to have daily rise of temperature (about 100°F.). Physical examination revealed slight dullness and râles in the right upper lobe, and the skiagram showed a light shadow in the right apex. No tubercle bacilli were found on repeated examination, but the sputum showed numerous *E. histolytica* though none was found in the faeces. A quick recovery followed administration of emetine.

Pulmonary amœbiasis may be primary or secondary. The primary form is rare, and according to Manson-Bahr (1940) it is caused by the entamœbæ reaching the lung by direct embolism from the intestinal wall and giving rise to formation of consolidated nodules, which later break down into small abscesses. According to Bunting (Stitt, 1942) the infection may also be carried from a thrombus in the hepatic vein containing amœbæ. Secondary pulmonary amœbiasis is more common and results from extension of the amœbic infection from the liver into the lung substance. It occurs in 10 (Kartulis) to 20 (Rogers) per cent of cases of liver abscess.

The following are records of two cases illustrative of pulmonary amœbiasis. Both were in-patients at the Carmichael Hospital for Tropical Diseases, Calcutta:

Case 1.—The patient was a Bengali woman, aged 24 years, admitted to the hospital for irregular fever of moderate degree, with cough and dull pain on the right side of the chest. The duration of the fever was two and a half months while that of the cough and pain was three weeks. The cough was at first dry and unproductive, but later she used to have slight expectoration. For some time prior to this illness she was complaining of lassitude, lack of appetite and loss of weight. Except for malaria four years ago, she had no illness of importance in the past. The family history was irrelevant.

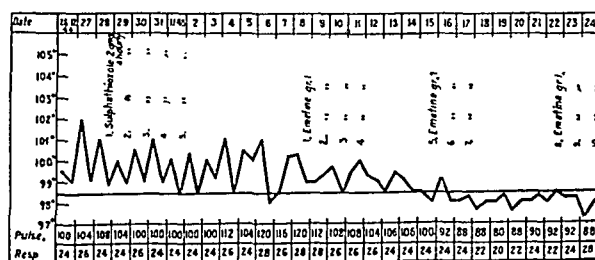


Fig. 2.—Temperature chart of case 1.

On admission, her temperature was 99°F., pulse rate 112, and respiration 28 per minute. She was thin built and weighed sixty-six pounds. Examination of the chest revealed an impaired percussion note on the right base with diminished breath sounds. The liver and spleen were not palpable. The heart was normal; blood pressure was 115/75. She was constipated, with a poor appetite and a slightly coated tongue. There was no glandular enlargement. The menstruation was scanty but regular.

Investigation.—The white cell count was 23,500 per c.mm. with 81 per cent polymorphonuclears, 15.5 per cent lymphocytes, 3 per cent large mononuclears and 0.5 per cent eosinophils. No parasites were seen in the blood. E.S.R. 40 mm. in one hour (Westergren). There was a moderate degree of anæmia. The sputum showed no acid-fast bacilli on repeated examinations.

A few cysts of *Giardia intestinalis* were found in the stools. The urine was clear. A skiagram of the chest (figure 1a, plate X) showed a small mottled opacity in the midzone of the right lung, the radiologist's comment being 'tuberculous infiltration'. On fluoroscopic examination, the patch appeared as faintly dull in the antero-posterior view but could not be clearly visualized in other positions. There was no upward enlargement of the liver, and the diaphragmatic movements were free.

Diagnosis and treatment.—The main clinical features of the case were fever, cough, lassitude, loss of weight and pain in the chest. These symptoms in a young woman along with a doubtful x-ray shadow were suggestive of pulmonary tuberculosis, but the marked leucocytosis and the absence of tubercle bacilli were against this diagnosis. An inflammatory lesion in the right lung was suspected, and she was put on sulphathiazole, but to no effect. It was then thought that it might be a case of pulmonary amebiasis, but repeated examination of the sputum did not reveal any *E. histolytica*. Emetine was tried as a therapeutic test, gr. 1 being given daily by injection. On the fourth day her pain in the chest increased and pleural friction sounds were audible in the right mid-axillary region. The drug was, therefore, discontinued. Now, however, she began to feel better and the temperature became normal in two days (see figure 2). The clinical improvement was so remarkable that it prompted us to give more emetine injections. All the symptoms rapidly disappeared, and there was progressive improvement in her well-being, appetite and weight. The leucocyte count came down to 8,000 per c.mm., and another skiagram taken within a fortnight showed complete disappearance of the opacity seen in the lung (figure 1b, plate X).

Case 2.—The patient, a Bengali woman, aged 24 years, was admitted under a different physician and was referred to us for fever. Her complaints were fever, cough and blood-stained sputum; duration two and a half months. There was no history of dysentery in the past, or contact with any tuberculous patient. She was thin, and no obvious abnormality was found on physical examination. Repeated sputum examinations failed to demonstrate tubercle bacilli, but *E. histolytica* was found on four consecutive days. Daily examinations of stools gave negative results, while a blood count showed only slight leucocytosis. The skiagram of the chest revealed no lung infiltration and the heart was of normal size. A fluoroscopic examination showed

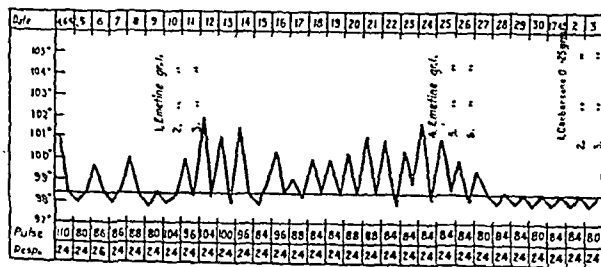


Fig. 3.—Temperature chart of case 2.

no upward enlargement of the liver and the movements of the diaphragm were free. A diagnosis of pulmonary amebiasis was made. Injections of emetine gr. 1 each were given daily, but after three days

the fever and hæmoptysis increased, and she refused to take any more. Ten days later she was persuaded to take 3 more injections after which the fever subsided (see figure 3). The hæmoptysis stopped but the cough persisted for some time. She was then given a course of carbarsone for 10 days during which she put on four pounds in weight.

Comment

Both the cases are of considerable interest and practical bearing. There was no history of dysentery in the past; there was no hepatic enlargement and no *E. histolytica* was found in the faeces. The fever, cough, pain in the chest, high leucocytosis, a mottled opacity in the lung field and the striking response to the therapeutic test with emetine were the main factors on which the diagnosis of pulmonary amebiasis was arrived at in the first case. In the second case fever and hæmoptysis were the presenting features; *E. histolytica* were found in the sputum, and there was good response to specific treatment. In both the cases there was aggravation of symptoms after the first few injections of emetine but the ultimate results were remarkable. It is well to remember this condition where an obscure fever with lung symptoms cannot be explained.

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BOVINE TUBERCLE BACILLI AND HUMAN EXTRA-PULMONARY TUBERCULOUS LESIONS IN THE PUNJAB

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PULMONARY tuberculosis in man is nearly always due to human type of *Mycobacterium tuberculosis*, but the primary extra-pulmonary type of tuberculosis is also caused by bovine type of bacillus, especially in children. The incidence varies in different countries.

In Scotland, for example, Mitchell (1914) found that 90.3 per cent of cases of tuberculous adenitis in children were due to the bovine type. Other workers have given different figures. The source of infection is usually milch cattle. The ætiological relationship of consumption of raw milk to the high incidence of the bovine type of infection in extra-pulmonary tuberculosis in children has been most clearly discussed by Price (1932). He examined 300 tuberculous children under 14 years of age. Of these 15 per cent were found to be infected with bovine type. All these children came from parts of Ontario outside Toronto, where milk was not pasteurized, and they all had been fed on raw

milk for some time. On the other hand, no case of tuberculosis of bovine origin was found in Toronto, where pasteurization had been compulsorily carried out since 1915.

The incidence of bovine type of infection has been reduced in some countries by systematic pasteurization of milk and the exclusion of tuberculous milch cattle. In India, people have a close association with cattle, especially in rural areas. In the Punjab, milk and its products form an important part of diet. In rural areas milk is not always boiled, and in some districts mostly raw milk is consumed. The excreta of animals especially cowdung is smeared on kitchen floors and is regarded sacred.

In India, only a few reports have been published bearing on the matter of bovine infection in human beings. Soparkar (1925) isolated 48 strains from extra-pulmonary sources, all of which belonged to the human type. He (1927) isolated 2 bovine strains and one avian strain from cases of adenitis in man, and another bovine strain in 1929 from a case of tuberculous adenitis in a girl. Ukil (1933) examined material from 60 cases, all of which were found to be due to human type of bacillus. Mallick *et al.* (1942) isolated 39 strains of tubercle bacilli from extra-pulmonary sources, 37 of which were found to be human type and 2 were still under investigation.

A definite parallelism between the frequency of tuberculosis in cattle and tuberculosis of bovine origin in human beings has been reported by several workers. In the Punjab, tuberculosis in cattle is reported to be fairly common. The following investigation is based on the study of human cases from Mayo Hospital, Lahore.

(a) *Selection of cases.*—Previous workers in India like Ukil (1933), Mallick *et al.* (1942), do not appear to have selected only those cases for investigation which were free from pulmonary infection. In the present investigation material was obtained from 52 cases, all declared to be free from pulmonary lesions by x-ray examinations. Particulars of 21 cases from which cultures of tubercle bacilli were obtained, are as follows:—

Diagnosis	Material obtained	Number of cases
Tuberculous osteo-articular disease.	Pus	12
Tuberculous lymphadenitis with abscess formation.	Pus	6
Tuberculous lymphadenitis	Glands	3
TOTAL ..		21

(b) *Age.*—The following table shows the number of cases in various age groups:—

1 to 5 years	2
6 to 10 "	1
11 to 20 "	8
21 to 30 "	8
31 to 40 "	Nil
41 to 50 "	1
Above 50 years	1

It will be evident from the above table that the maximum number of cases were seen in the 11 to 20 and 21 to 30 age groups.

(c) *Sex.*—Out of 21 cases 10 were in females and the rest in males.

(d) *Residence.*—Fifteen out of 21 lived in urban areas.

(e) *Habits regarding taking of milk and its products.*—Out of 21 cases, 6 patients had been taking boiled milk as a rule, but even they were not absolutely sure that they had never taken raw milk in any form. Fifteen patients took both boiled and raw milk especially in the form of lassi, i.e. water mixed with a little milk.

(f) *Bacteriological findings.*—The following four media were used in this investigation:—

1. Simple Dorset's egg medium.
2. Glycerinated Dorset's egg medium.
3. Löwenstein-Jensen medium (glycerinated).
4. Löwenstein-Jensen medium without any glycerine.

A fair amount of water of condensation was left at the bottom of the tubes to prevent the media drying up in the hot dry summer.

Twenty-one strains were isolated, all of human type. Two were doubtful but were confirmed as of human type by Dr. F. C. Minett of the Imperial Veterinary Research Institute, Mukteswar.

Colonies in the culture of *Mycobacterium tuberculosis* may assume any shape and size. They may be grey, greyish-white, orange or yellowish. They may even be bicoloured, e.g. in case no. 7 the colonies were greyish-yellow with a margin of light orange colour round about. The surface of the colonies may be smooth or granular, sticky or dry. Sometimes the colonies were difficult to be detached. The time taken for the colonies to grow may be as short as 15 days.

Discussion

The source of bovine infection in man is milch cattle. According to the reports of veterinary investigation officers in different provinces, the incidence of tuberculosis is greatest in the Punjab, but if more work is done in urban areas in other provinces, higher figures may perhaps be found. For example, according to the annual report of the Imperial Veterinary Research Institute, Mukteswar, for the year 1939-40, the incidence of tuberculosis amongst bullocks of Puri Municipality in Orissa was over 80 per cent.

In this province (Punjab), the earliest work is that of Taylor (1918) in the years 1915-17. He found the incidence of infection in the slaughtered animals to be from 3.3 to 3.5 per

cent. Soparkar and Dhillon (1931) reported the incidence of infection in slaughtered animals as follows:—

	Per cent
Cows	21.3
Bullocks	31.6
Buffaloes	23.6

Reference may also be made to the investigations carried out by the veterinary investigation officers in this province.

During the period 1938-45, 7,317 animals including cows, buffaloes and bullocks were subjected to tuberculin tests, and it was found that 135 animals reacted positively giving a percentage of 1.84. Out of 50 cows tested at the Government Cattle Farm, Hissar, 15 were found to be positive reactors, giving a percentage of 30. In Montgomery Dairy Farm, out of 137 animals, 22 were positive and out of 26 buffaloes, 15 were positive (57.69). During the year 1941-42, examination of carcasses of 242 cows, 175 buffaloes, 43 goats, 35 sheep showed that 18 cows had localized lesions in bronchial and mediastinal glands, and one had miliary tuberculosis. Nine buffaloes showed tuberculous lesions confined to lymphatic glands, one goat showed lesions in the lungs. Out of 177 animals of hill breed tested during the year 1943-44, none showed any positive reaction.

Out of 1,234 animals tested by Mallick *et al.* (1942) at Amritsar, about 23 per cent were found to be positive reactors. Nanda, using a standard tuberculin, subjected a large number of animals to tuberculin test at the Government Cattle Farm, Hissar. The tests were carried out at six-monthly intervals and the total heads of cattle varied between 3,000 and 4,000. The percentage of positively reacting animals varied from 20.25 in the first test to 1.92 in the eighth test.

From the above reports it will be observed that the percentage of tuberculous animals in the hill breeds and the rural areas is negligible, but the incidence is very high in dairy farms. The incidence of infection in buffaloes at Montgomery is very alarming (57.69 per cent). Broadly speaking there is fair incidence of the disease in cattle in this province, but investigations have shown that the lesions found in the animals are quite different from those found in other countries. The lesions found here are retrogressive in type, and usually the lymph glands are involved, and the disease is much more chronic and localized than in other countries. As it is a rarity to find cavities in the lungs, the sputa of these animals seem to be harmless. Enquiries from the Veterinary College, Lahore, revealed the noteworthy information that not more than half a dozen cases of tuberculous mastitis have been seen in this province.

The main vehicle responsible for carrying infection from the infected animals to human beings is milk and its products. Joshi (1914) working in Bombay during 1910-12, found, by animal experiments, that none of the 674 samples of milk examined contained tubercle bacilli. Mallick *et al.* (1942) examined 101

samples of milk taken from animals which reacted positively to tuberculin in Amritsar, but none of them showed any tubercle bacilli. According to the report of the Veterinary Investigation Officer for 1943-44, milk from 78 cows which had reacted positively to tuberculin, was examined for the presence of tubercle bacilli, but none was found.

Animals having tuberculous ulcers in the intestines are bound to pass tubercle bacilli in their excreta. In this country, the faeces of animals have not been examined systematically, but as intestinal lesions have not been observed, there seems to be no possibility of the spread of infection by this means. Similarly as open cases of tuberculosis have rarely been seen in this country, infection cannot be transmitted to man by inhalation. For these reasons no useful purpose will be served by undertaking an investigation among human beings for the occurrence of infection caused by the bovine type of organism. An enquiry into the incidence of udder infection and the presence of tubercle bacilli in milk and excreta of tuberculin reacting animals, is certainly indicated.

Summary

1. Twenty-one strains of *Mycobacterium tuberculosis* were isolated from extra-pulmonary sources from patients who showed no lesions in their lungs. All the strains were found to be of human type.

2. Colonies of cultures may assume different shape, size, colour, etc.

3. There is no evidence to show that in the Punjab, which is reported to have the highest rate of infection in cattle, the bovine type of bacillus plays any part in the causation of extra-pulmonary type of tuberculosis in human beings. This may be due to two factors. Firstly, the incidence of infection in cattle, except in farms and cities, is negligible. Secondly, udder infection in cattle is rare, and animals suffering from other types of lesions do not pass tubercle bacilli in milk or in their excreta. Reference has also been made to the absence of tubercle bacilli in the milk of 179 animals which reacted positively to tuberculin.

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TROPICAL EOSINOPHILIA : SOME FURTHER OBSERVATIONS

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Geographical distribution.—Cases of tropical eosinophilia reported so far have been mostly from India and Ceylon. A careful survey of the literature shows that the condition is more widespread geographically than is at present realized. Thus, Saint Etienne (1938) records a case of massive eosinophilia,

various types seen in one year by Mathew (personal communication) at the Kochuvareed Tuberculosis Clinic, Trichur (South-west India), no less than 134 (9.7 per cent) were cases of 'eosinophil lung.' This is in close agreement with figures given by Viswanathan (1945) for a different area, somewhere in North India, viz, 85 cases out of 946 admitted for various respiratory diseases. The syndrome, therefore, merits further attention by virtue of its wide distribution and high incidence in certain localities.

Diagnosis.—The general trend of opinion recently has been to regard it as a separate clinical entity. There has, however, been some pertinent criticism of this view. It is based chiefly on the variability of symptomatology and, to some extent, on the fact that cases which definitely are not examples of the condition, are being included as such, uncritically. A clear definition of the diagnostic criteria is sure to be helpful to workers on the subject. The following case reports illustrate some of the difficulties arising in diagnosis.

TABLE I

Sex and age	1	2	3	4
	M., 17	F., 5	F., 20	M., 22
Previous history of allergy ..	Asthma 4th to 12th year.	Asthma 3rd to 5th year.	Asthma in childhood.	Asthma in childhood.
Duration of symptoms	6 months	3 months	2 months	Several years
Fever	+	+	Nil	Nil
Cough	+	+	+	Nil
X-ray appearance	+	Nil
Total W.B.C./c.mm.	49,500	13,000	10,000	9,800
Eosinophil per cent	79	25	43	12
Eosinophils/c.mm.	39,100	3,250	4,300	1,176
E.S.R. 1 and 2 hours in mm. ..	39, 86	24, 40	10, 30	2, 3
Wassermann	Strongly +	Strongly +	Negative	Negative
Kahn	Strongly +	Strongly +	Negative	Negative
Arsenical treatment and number of injections. ..	N.A.B. 4; Mapharside 3.	Stovarsol acetyl-arsan 4.	N.A.B. 2	Soamin 8
Result	Cured	Almost normal	No improvement	No improvement
Eosinophils/c.mm. after treatment ..	2,100	620	Not done	1,200

82 per cent out of a total white cell count of 22,300/c.mm. from Tong King, China. Bass (1941) refers to 7 cases with a similar picture from America and Havana. Ritchie (1944) describes tropical eosinophilia in an African patient from Tanganyika. Parsons-Smith (1944) reports it in an English airman after 10 months' stay in Egypt. Treu (1944) mentions it in a Chinese patient from Singapore. McGuire (1945) during a discussion on periarteritis nodosa, asthma and hypereosinophilia, refers to two American soldiers who developed tropical eosinophilia after staying in an island in South-west Pacific. Hirst and McCann (1945) report another case from Samoa, South Pacific.

Within India itself, it seems to be a common condition in many areas. Thus, out of 1,383 cases of respiratory diseases of

The two cases in table II have been reported in detail merely to show the danger of attempting a diagnosis on the blood picture alone. There is nothing in their history, signs or symptoms even to suggest, much less support, a diagnosis of tropical eosinophilia. While the initial eosinophilia in case 2 may be due to helminthic infection, the 600 per cent increase in total eosinophils within a fortnight in that case and the 350 per cent increase in case 1 are apparently due to the insulin injections. Soluble insulin was used in both cases but of different manufacture, viz, Lilly and Squibb. The possibility of insulin, liver extract and other injections, such as digitalis, camphor, etc., being responsible for eosinophilia must, therefore, be considered in diagnosis.

Coming to the cases in table I, case 4 with a total white cell count of 9,800/c.mm., 12 per

TABLE II
Eosinophilia produced by insulin

Sex and age	1		2	
	F., 21		F., 38	
Previous history of allergy ..	<i>Nil</i>		<i>Nil</i>	
Chief complaint ..	Underweight		Underweight	
Other complaints ..	Anorexia		Roundworm infection	
Insulin injections, number ..	12		10	
Insulin injections, total units ..	180		105	
Total W.B.C./c.mm. ..	Before	After	Before	After
Eosinophil per cent ..	6,500	14,000	8,300	16,000
Total eosinophils/c.mm. ..	2	33.5	21	63
Interval between end of treatment and second count.	130	4,690	1,743	10,080
Eosinophil per cent later ..	21 days		4 days	
	58 per cent after 3 months		Not done	
	60 per cent after 4 months			

cent eosinophils and E.S.R. of 2 and 3 mm. can safely be diagnosed as asthma. Case 3 with 43 per cent eosinophils is more difficult. The total count of 10,000/c.mm., E.S.R. 10 mm. in first hour, negative W.R. and Kahn, and lack of response to arsenic are against the diagnosis of tropical eosinophilia but in favour of that of asthma. Cases 2 and 1 had asthma in their childhood, like cases 4 and 3, but unlike many of the cases previously reported. In addition, in case 2, the father of the patient gave a history of asthma when young. The family and personal history of asthma and the fact that the total white cell count of 13,000/c.mm. and eosinophil per cent of 25 both not very high, are in favour of asthma. There are also no lung signs and the x-ray picture is normal. But there is a typical history of fever, cough and loss of weight (features absent in cases 4 and 3). The E.S.R. is decidedly high for a child, being 24 mm. in 1 hour; and finally, the blood gives strongly positive Wassermann and Kahn reactions. That it is not a congenital condition is clear from the fact that the specimens of blood of both parents are W.R. and Kahn negative. After 20 tablets of stovarsol by mouth, the patient's serological reactions are reversed, both W.R. and Kahn giving negative results. Here is a case where the diagnosis cannot be said to be beyond doubt, but the balance of evidence is decidedly in favour of tropical eosinophilia. In case 1, however, despite the history of early asthma, the diagnosis is clear. The fever, cough, lung signs, x-ray picture, total white cell count of 49,500/c.mm. and total eosinophil count of 39,100/c.mm., E.S.R. of 39 mm. in 1 hour, the strong positive W.R. and Kahn reactions and the response to arsenical treatment combine to make this a typical picture of tropical eosinophilia, in a previously asthmatic subject.

When we are confronted with eosinophilia in a patient, it is necessary to eliminate several clinical possibilities, e.g. effect of injections

like insulin, liver extract, etc., helminthic infections, specially trichinosis, atypical leukæmias and Hodgkin's disease, periarteritis nodosa, allergic conditions and affections of the skin. Two other conditions, viz, Löffler's syndrome and familial eosinophilia may be more difficult to separate from tropical eosinophilia. Diagnosis is easy where the typical symptomatology is present, as in case 1. In its absence, a total white cell count below 10,000/c.mm. eosinophil per cent below 20 and E.S.R. normal or lower, should be regarded as ruling out the possibility of tropical eosinophilia. A total white cell count between 10,000 and 15,000, eosinophil per cent below 25 and E.S.R. normal or slightly raised, justify consideration of the syndrome as one of the diagnostic possibilities, along with others enumerated above. If the total eosinophil count is 5,000/c.mm. and above, i.e. 25 per cent and more of a total white cell count of 20,000/c.mm., tropical eosinophilia should be considered first in the diagnosis. If the typical symptomatology is present, the diagnosis is beyond doubt. Even if it is not present, a very high E.S.R. and positive Wassermann and/or Kahn reactions justify such a diagnosis and the consequent therapeutic trial with arsenic. An initial exacerbation with subsequent rapid improvement, clinically after arsenical treatment, will practically settle the diagnosis.

Inoculation experiment.—Menon (1945) suggested that tropical eosinophilia may be an infective condition, resembling infectious mononucleosis, atypical pneumonia, etc. Other workers also have held a similar view, but, so far, no experimental evidence has been offered either for or against it.

Intraperitoneal injections of blood from cases of tropical eosinophilia were given to guinea-pigs. Specimens, either oxalated or diluted with normal saline and sent by post were found unsatisfactory due to degenerative changes. Animals injected with such blood, however, did

not show any response different from that shown by control animals, *e.g.* guinea-pigs 3 and 4. Blood from case 1 (table I) was collected in equal quantity of normal saline, mixed well by shaking for 5 minutes and taken by special messenger to the institute where it was used within 6 hours. Two guinea-pigs, numbers 1 and 2, were each given intraperitoneally 1.25 c.cm. of blood in equal amount of saline. Guinea-pigs 3 and 4 were used as controls and injected similarly with blood from a normal person and from an asthmatic patient with high eosinophilia (25 per cent), respectively. Table III gives the figures for weight and leucocytic changes in the four animals while table IV gives a more detailed account of the changes in guinea-pigs 1 and 2.

tration of the alveoli with mature eosinophil cells.

The similarity in response of guinea-pigs 1 and 2, *viz.* the high secondary leucocytosis with neutrophil predominance, the initial eosinophilia, the loss of weight and the duration of 10 days, is in marked contrast to the absence of changes in guinea-pigs 3 and 4 after 10 days. The possibility of anaphylactic phenomena causing the changes may be considered; but against it are: (1) only one injection of blood was given to each animal, (2) leucopenia—and not leucocytosis—is the usual finding in anaphylaxis, according to Widal, Joltrain, and others (Urbach, 1944), and (3) the Prausnitz-Kuestner technique of passive transfer has consistently shown itself to

TABLE III

Guinea-pigs		Weight in grammes	Total W.B.C./c.mm.	Neutrophils	Eosinophils	REMARKS.
1 (blood from case 1 injected)	At start	450	7,500	2,850	1,690	Died.
	On 10th day	295	48,000	37,680	240	
2 (blood from case 1 injected)	At start	480	10,400	2,600	832	Recovered.
	On 10th day	395	28,600	16,016	1,573	
3 (blood from a normal person injected).	At start	515	15,000	3,150	4,200	No change.
	On 10th day	525	12,000	3,120	4,000	
4 (blood from an asthma patient injected).	At start	505	14,200	4,118	2,272	No change.
	On 10th day	512	14,000	5,180	2,660	

TABLE IV

	Guinea-pig 1				Guinea-pig 2			
	Weight in grammes	W.B.C./c.mm.	Neutrophils	Eosinophils	Weight in grammes	W.B.C./c.mm.	Neutrophils	Eosinophils
Before injection ..	450	7,500	2,850	1,690	480	10,400	2,600	832
1st day after injection ..	420	21,200	11,448	6,360	440	22,500	10,575	2,250
2nd " " " "	395				420			
3rd " " " "	380	13,000	8,450	910	420	12,900	4,515	1,677
4th " " " "	382				420			
5th " " " "	370	9,650	6,080	1,351	400			
6th " " " "	368				408	15,200	7,600	3,040
7th " " " "	358	45,800	23,130	2,980	408			
8th " " " "	360				390	16,000	7,680	1,280
9th " " " "	345	48,500	37,000	400	395			
10th " " " "	295	48,000	37,680	240	395	28,600	16,016	1,573
15th " " " "	430	9,200	2,300	1,500

Specimens of blood were collected from the ear-lobes of the animals and their weights taken daily at the same time, *viz.* between 3-0 and 3-30 p.m., before their evening feed. The counts were done by the author, using a standard technique and the pipettes used were subsequently checked against 'certified' pipettes and found to be correct. Percentage figures were obtained by differential counts of 400 white cells from each slide.

Post-mortem examination of the tissues from guinea-pig 1 revealed no significant change except that sections of the lungs showed infil-

be of no avail in relation to lower animals (Urbach, *loc. cit.*). We have, therefore, to assume that the blood of the patient contains material which is responsible for these changes on animal inoculation. Whether it is an infective organism or only a metabolic product derived from the organism or the patient's tissues is still open to discussion. It has to be admitted that no conclusion can safely be drawn from a single experiment. The non-availability of fresh blood from typical cases has prevented the further work necessary to confirm these findings. However, the results obtained appear

to be in agreement with the theory of an infective origin of the syndrome.

Summary.—(1) Tropical eosinophilia has a wider distribution geographically and a higher incidence in certain localities than are now recognized.

(2) An attempt has been made to define clearly the findings essential for diagnosing it.

(3) Experimental evidence based on guinea-pig inoculation with blood is offered in support of an infective origin of the syndrome.

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STUDIES OF RINGWORM

Part III

PROPHYLACTIC MEASURES

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and

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(From the Medical Mycology Enquiry, Indian Research Fund Association at the School of Tropical Medicine, Calcutta)

IN the tropics ringworm infection of the body is not only common but difficult to avoid and more difficult to cure. In any skin outpatient department the number of cases of dermatomycosis is quite large. In Calcutta, 20 per cent of the total number of patients with skin disease come for the treatment of ringworm infection, i.e. about 2,000 new cases every year. To this may be added quite an appreciable number who come for treatment of some other complaints but have the ringworm infection as well, and many others who suffer from ringworm but do not come for treatment. Some have chronic infection with the nails and a large area of the body affected, and have given up treatment in despair, others overlook the early infection or neglect the treatment, as the infection does not cause much inconvenience.

Infection of the feet, between the toes, deserves special mention. It has been our experience that even intelligent and educated people overlook or often neglect this infection as it does not cause much trouble. Even when this mild infection begins to cause inconvenience they try to belittle it and apply some dusting powder or strong antiseptic lotion to kill the so-called 'Bengal rot' or 'Hongkong foot' with the result that, after a couple of years or more, there is a sudden outburst of blisters involving the feet and the hands causing severe pain and total disability for months. This condition is not only very painful and distressing but is persistent with many relapses, due to the sensitization of the skin.

To avoid all these unpleasant and sometimes serious complications it is advisable to adopt prophylactic measures. This is especially important for those in whom the infection has been controlled but not eradicated and more especially for foreigners coming to this country from more temperate climates.

From time to time various prophylactic measures have been recommended, but so far none of them has been found to be very useful or entirely suitable. Various dusting powders have been recommended, but dusting powders by themselves are of limited use; moreover, they are often messy. Lotions and baths are often either so strong as to cause irritation of the skin or else too weak to be effective. Some drugs, commonly used in the treatment of ringworm, are undoubtedly good parasitocides but many of these are irritants to the skin (e.g. chlorine solutions, mercury salts) or they are coloured and spoil the clothes (the aniline dyes and chrysophanic acid).

In trying out the various drugs and chemicals as prophylactics the following points had to be taken into consideration:

(1) The drug must be easily available in India—this was particularly so in war time when many drugs and chemicals were either not at all available or available in very small quantities.

(2) They should be easily soluble in water if a lotion is to be made.

(3) They should be colourless, or if coloured, the colour must be light and easily removable from the clothes and the skin.

(4) They should not be irritant to the skin even after prolonged use.

(5) They should not be harmful if absorbed.

(6) They should not be corrosive to the clothes or to the skin.

(7) They should be such as to be easily applied, not messy and not sticking to clothing.

(8) They should not have objectionable smell.

There were few drugs which would answer all these requirements. The drugs selected were tested *in vitro* for their fungicidal properties, and those which appeared to have fairly good fungicidal properties were then put to

clinical test. The clinical tests were made on patients susceptible to the fungus infection, that is, who had been constantly suffering from the infection or who had the infection recently and were clinically cured.

The fungicidal properties of the drugs selected were tested against *Epidermophyton floccosum*. *E. floccosum* was selected as the test fungus as this is the most common fungus found in this country. A fine emulsion of the fungus was made in sterile normal saline solution in a glass-stoppered phial with the help of sterile glass beads, by vigorous shaking till the emulsion assumed a uniform standard opacity. A known quantity of this emulsion was then mixed with a known quantity of the solution of the drug to be tested, in different dilutions, and the mixture was shaken well. After the scheduled interval, a loopful of this mixture of the fungus and drug solution was inoculated in the Sabouraud's peptone-glucose-agar medium, and kept at the room temperature for 4 days and any growth noted.

The full details of this test were published from this department in the *Indian Journal of Medical Research**. Every test was of course repeated and control tests were carried out.

Two sets of experiments were done—one with the watery solution of the drug and another with the alcoholic solution. Twenty-five per cent alcoholic solution was taken as the standard as it does not evaporate too quickly.

In all cases the alcoholic solution proved to have a better fungicidal action than the watery solution.

The results are briefly tabulated here.

have also a keratolytic action in destroying the epithelial cells on which the fungi grow. Used as a prophylactic measure these proved to be of some value in those who carry very mild infection but for general prophylactic measures these drugs cause irritation to the skin, exfoliation and sometimes excoriations. Prolonged use of salicylic acid and benzoic acid has been known to cause dermatitis.

Glacial acetic acid stood first in its fungicidal properties in the group of drugs tested. When brought in contact with the fungus, it killed the fungus in the watery dilution of 1/1000 in one minute, and 1/2000 in 5 minutes. In 25 per cent alcoholic solution it killed the fungus in one minute up to 1/4000 dilution, and up to 1/5000 dilution in 5 minutes. Weak glacial acetic acid solution is non-irritating to the skin, non-corrosive and harmless if used for a prolonged period. It is non-corrosive and non-staining to the clothes. A clinical trial for the last two years has given a uniform satisfactory result in preventing the relapses or getting fresh infections. One of the authors was a subject of the infection in the toes and groin for several years, and he has been able to keep himself free from symptoms for the last two years by taking these prophylactic measures. Stock solutions of glacial acetic acid with 25 per cent alcohol were prepared in different dilutions and results of the clinical trial are given here: A 1 per cent solution was found effective in softer parts of the skin but not in the susceptible parts such as the toes and the crural region; a 2 per cent solution was found effective in preventing a fresh infection but not in

Drugs	MAXIMUM FUNGICIDAL DILUTIONS			
	Watery solution		Alcoholic solution (25 per cent alcohol)	
	1 minute	5 minutes	1 minute	5 minutes
Glacial acetic acid	1/1000	1/2000	1/4000	Over 1/5000
Salicylic acid	1/500	1/1000	1/3000	1/4000
Benzoic acid	1/500	1/500	1/3000	1/3000
Tartaric acid	Less than 1/50	1/100	1/1000	1/2000
Liquid phenol	1/100	1/300	1/2000	1/2000
Thymol	1/400	1/500	1/2000	1/2000
Formaline	1/400	1/500	1/2000	1/2000
Tincture iodine	1/400	1/500	1/400	1/500

From the table above it will be seen that in this series three drugs proved to have good fungicidal properties, namely, (1) glacial acetic acid, (2) benzoic acid, and (3) salicylic acid.

Of these, the last two are well-known drugs used in the various preparations for the treatment of ringworm infection. But their main action is in rapidly peeling off the surface epithelium and along with it the fungus. They

preventing relapse of an old infection where the infection persists in cold weather without causing any symptoms and flares up in hot damp weather; and 4 per cent solution was found generally effective as a prophylactic.

A 4 per cent solution (20 ml to 1 oz.) has been used as the stock solution in all later experiments.

The prophylactic method

In the tropics two baths a day have always been recommended especially in hot weather.

* 25, 3, January 1933, p. 603, and 29, 1, January 1941, p. 23.

This keeps the body surface clean and prevents many fungal and bacterial infections of the skin. Where two baths are not possible (e.g. in the army) one bath after the day's work is imperative.

After the bath, the body surface should be wiped dry with a towel with special attention to the susceptible parts, which are the axillæ, the crural region, the perineum, the inner sides of the thighs and the skin in between the toes. If any infection is suspected, a separate towel should be used for the suspected places, or better still a little cotton-wool, which is discarded after use. Some fresh cotton-wool is then soaked in the solution and rubbed gently in the affected parts, beginning from the axillæ and finishing with the toes. The axillary area may be omitted in non-susceptible persons as this is not so frequently affected as the groin or toes. The same cotton-wool is used for all the parts at one time. The rubbing should not be vigorous but gentle and firm.

The method described above is not only simple but easy to carry out, and does not require the help of other persons. No elaborate apparatus is needed; one towel, a bottle of the solution and a packet of cotton-wool are necessary. One pound of the solution and 4 oz. of cotton-wool should last at least 4 months.

The cost of glacial acetic acid is not prohibitive; one pound costs about Rs. 4 and one pound of the acid will make up 24 pounds sufficient for 12 men for one full year.

The prophylactic measures should be started as soon as the hot weather starts. In Calcutta and south India it should be started from the month of March and continued till the end of October, whereas in north-west India the period should be from April to the end of October. But the practice can be continued throughout the whole year.

The prophylactic measures mentioned above have given uniformly satisfactory results in preventing ringworm infection in all the test cases. Most of the test subjects were susceptible individuals showing active infections every hot weather, and some of them carrying active lesions throughout the year. The active lesions were first treated by the usual methods till they were clinically cured and then the prophylactic measures applied. All who carried out the measures reported good results and freedom from relapses. An additional measure, both as prophylactic and also for comfort, is to dust over lightly some dusting powder containing kaolin and starch, the usual formula being:—

Boric acid powder	} each 2 drachms.
Zinc oxide	
Kaolin	
Starch	

The powder absorbs the moisture and keeps the parts comfortable, but should be used very lightly.

Summary

1. Several drugs were tested as prophylactic agents against ringworm infection.
2. A 4 per cent solution of glacial acetic acid in 25 per cent alcohol was found effective in preventing ringworm infection.
3. In the tropics the prophylactic measures should be taken throughout the nine months from March to November.

CULTURE MEDIUM FROM GROUNDNUT MEAL

Part II

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and

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In a recent paper (Basu, Sen and Sen Gupta, 1945) we have shown that groundnut meal affords a culture medium for the growth of various intestinal organisms when it is digested with some proteolytic enzyme. The hydrolysate when further admixed with a trace of liver extract gives still better results. The latter observation led us to work on the growth of other delicate organisms, and the experimental data obtained are recorded in this paper.

The broth.—A solvent-extracted meal as obtained by the process described by Basu and Sen Gupta (1944) was digested by papain in the presence of sodium thiosulphate according to the method previously described by us (Basu, Sen and Sen Gupta, 1945), and incorporated with 2 per cent as well as 5 per cent liver digest. The pH was adjusted to 7.8, and the oxidizable matter was 0.75 per cent.

Bacteriological tests.—The following organisms were used to study the growth-promoting power of the broth: pneumococcus types I, II and III; influenza bacillus; gonococcus; *Streptococcus hæmolyticus* and meningococcus. The results are recorded in the table.

In working with the bazaar meal we thought that the processing during the extraction of groundnut oil by hydraulic press or the expessor process might destroy and/or produce deterioration in the nutrient substances of the nut, and that the broth obtained from it might not be suitable for the growth of the more susceptible organisms. Consequently, medium was also made from groundnut meal made from fresh groundnut after extraction of the oil with low boiling solvent (petroleum ether). From the table it would be noticed that it offers no special advantage over the less costly and easily available bazaar meal for the growth of organisms like pneumococcus type, I, II and III, *Streptococcus hæmolyticus* and meningococcus. Neither the gonococcus nor influenza bacillus grew in any of the above media,

TABLE

Media	GROWTH AFTER 24 HOURS OF INCUBATION AT 37°C.						
	Pneumococcus type			Influenza bacillus	Gonococcus	<i>Streptococcus hæmolyticus</i>	Meningococcus
	I	II	III				
Groundnut meal (bazaar) in agar slants.	+	+	+	—	—	+	+
Groundnut meal (solvent extract) in agar slants.	+	+	+	—	—	+	+
Groundnut meal (solvent extract) with 2 per cent liver extract.	+	+	+	—	—	+	+
Groundnut meal (solvent extract) with 5 per cent liver extract.	+	+	+	—	—	+	+

+ Satisfactory growth compared to routine media.
 — No growth.

as was expected. The activation of the enzyme by suitable reducing substances like sodium sulphide or thiosulphate is, however, necessary as the substrate (meal), unlike meat, does not contain a reducing sulphhydryl group (cf. Gottschall, 1944).

Conclusion

Groundnut meal when digested with papain offers a hydrolysate for use as culture medium.

The hydrolysate with a trace of liver digest added is found to be a suitable nutrient broth for the cultivation of organisms like the pneumococcus, the streptococci and the meningococcus.

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THE 'LIFE' OF LIQUID PREPARATIONS OF ADRENALINE UNDER ORDINARY STORAGE CONDITIONS IN INDIA

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 and

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Introduction

IN the course of an all-India survey of the quality of drugs and medicinal chemicals undertaken at the Biochemical Standardization Laboratory during 1937-1941, Mukerji and Dutta (1943) noted that several preparations of liquor adrenalinae hydrochloridi, B.P., 1932, which purported to be a 1 in 1,000 solution, were markedly weaker than this when examined on the blood pressure of pithed cats,

a method of assay for adrenaline advocated by Burn (1937) and also recommended (with slight modifications) by the U.S.P., XII, 1942. Since then, potency tests have been carried out in another group of 200 samples of liquor adrenalinae hydrochloridi and liquor adrenalinae tartratis, both of indigenous and foreign manufacture, and the results left little room for doubt that adrenaline solutions deteriorated rather quickly on storage under conditions ordinarily available in Indian pharmacies and laboratories (Bose, Dutta and Mukerji, 1942). With a view to preventing the use of adrenaline solutions of low potency, and in view of preliminary observations on the keeping quality of these adrenaline solutions, a tentative suggestion was made that a 'date of expiry' of potency of approximately one year from the date of manufacture should be put on the label of all liquid preparations of adrenaline marketed in India. In the present paper, a systematic study of the rate of deterioration of adrenaline solutions stored under ordinary laboratory conditions for a period extending from four months to four years has been undertaken to see how far the previous recommendation regarding 'dating' of liquid preparations of adrenaline in India could be considered valid, and whether such a departure from the usual practice should be insisted upon in this country.

The stability of adrenaline solutions is naturally a matter of vital importance to all medical practitioners, as this is one of the most essential of remedies for emergency use. Any major variation in potency of this preparation may mean all the difference between the life and death of a patient.

Experimental

By employing methods already reported (Bose, Dutta and Mukerji, *loc. cit.*), 26 samples of liquor adrenalinae hydrochloridi and 40

samples of liquor adrenalinae tartratis, received through the official channels, were tested for potency. These samples were then marked and set aside on an exposed laboratory shelf, in a condition more or less similar to that ordinarily available in most dispensaries, druggists' counters and pharmacies in this country. Samples were taken out at repeated intervals between four months and four years for rechecking, the assay method remaining constant in all cases.

All the samples were prepared by the local manufacturing firms according to instructions issued from the office of the Director-General, Indian Medical Service. Liquor adrenalinae tartratis was prepared because it was reported from Great Britain to possess better stability than liquor adrenalinae hydrochloridi of the B.P., 1932. From previous experience regarding the comparatively poor stability of adrenaline solutions in tropical climate, the use of an anti-oxidant, such as sodium metabisulphite (not recommended in the B.P., 1932), was enjoined in the preparation of all these samples.

The formulæ of the solutions employed are given below :

Liquor adrenalinae hydrochloridi

Adrenaline	1 gm.
Chlorobutol	5 gm.
(Or chlorocresol	1 gm.)
Sodium chloride	9 gm.
Dilute hydrochloric acid	3 millilitres
Sodium metabisulphite	1 gm.
Distilled water sufficient to produce	1,000 millilitres

Liquor adrenalinae tartratis

Adrenaline	1 gm.
Chlorobutol	5 gm.
(Or chlorocresol	1 gm.)
Sodium chloride	9 gm.
Tartaric acid	0.65 gm.
Sodium metabisulphite	1 gm.
Distilled water, freshly prepared, sufficient to produce	1,000 millilitres

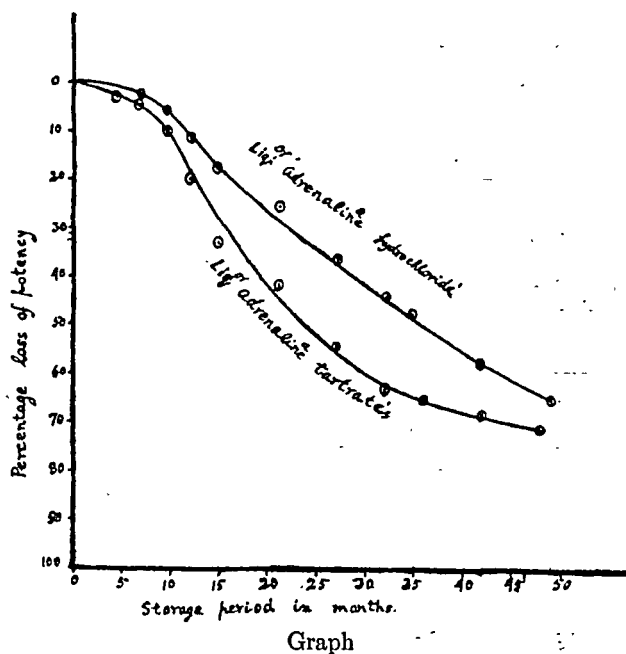
The methods of preparation and sterilization insisted upon were : 'Dissolve the chlorobutol or chlorocresol and the sodium chloride in 900 millilitres of boiling distilled water, cool, add the tartaric or the hydrochloric acid, as the case may be, dissolve the adrenaline and the sodium metabisulphite in the mixture and add sufficient distilled water, recently boiled and cooled to produce the required volume. Bottle in one-ounce sterile bottles, close the bottles with non-absorbent cotton-wool plugs, and sterilize them at 80°C. for one hour. Remove the cotton-wool plugs and close the bottles with sterile rubber corks. Place a sterile viscose cap over the corks'.

The containers must comply with the test for limit of alkalinity of glass in the B.P., 1932 (Mukerji and Dutta, *loc. cit.*).

Results

Table I shows the results obtained with liquor adrenalinae hydrochloridi samples, and table II with the adrenaline tartrate samples. In each case, the character of the original solution, the pH ranges, the average initial potency, the average period of storage and the loss of potency at the end of the observational period are indicated. In the graph the percentage loss of potency has been plotted against the various storage periods.

From the tables it would be evident that the average 'life' of liquid preparations of adrenaline under ordinary storage conditions is about 10 months, the extreme figures varying from 8½ to 11 months. From the graph, it would appear that the rate of deterioration is rather slow during the first year and gradually becomes more rapid in the next two years, after



which it tends to become slow again, when the loss of potency reaches about 55 to 60 per cent of the original strength. At this stage, the curve tends to form a more or less straight line, indicating that there is hardly any further loss of potency. Following fairly long storage, a pinkish or brownish colour usually develops in most samples, followed in some cases by precipitation of very minute black particles. This change of colour, though significant, cannot always be correlated with a loss of potency, though the formation of a precipitate, according to our observation, can be definitely associated with marked deterioration.

Another point which also emerges from the tables and the graph is that there is nothing to choose between liquor adrenalinae hydrochloridi and liquor adrenalinae tartratis, as far as deterioration is concerned under Indian conditions. Liquor adrenalinae tartratis, contrary to expectations, did not show any better stability than liquor adrenalinae hydrochloridi.

TABLE I
Samples of liquor adrenalinae hydrochloridi

Number of samples tested	Character of the original solution	pH range	Average initial potency with standard deviation	Storage period in months	Average storage period in months	Character of the solution after storage	pH range after storage	Average percentage of loss of potency after storage plus standard deviation
1	Colourless, clear.	1.8	100.0% \pm 0.0	6	6	Colourless, clear	1.8	3.0% \pm 0.0
3	Do.	1.8 to 2.0	100.0% \pm 0.0	8 to 10	9	Do.	2.0	7.3% \pm 1.3
7	Do.	2.0	100.5% \pm 1.2	11 to 13	12	Do.	2.0	12.2% \pm 4.2
4	Do.	2.0	98.5% \pm 1.7	14 to 16	15	Do.	2.0	18.3% \pm 4.2
6	Do.	1.8 to 2.0	99.7% \pm 7.1	19 to 23	21	Brownish, tinge, clear.	2.0	25.1% \pm 4.1
8	Do.	1.8 to 2.0	98.5% \pm 1.1	25 to 29	27	Do.	2.0	37.6% \pm 10.5
13	Do.	2.0	101.9% \pm 5.1	30 to 34	32	Do.	2.0	44.7% \pm 3.1
5	Do.	1.8 to 2.0	99.5% \pm 3.4	35	35	Do.	2.0	48.2% \pm 2.4
3	Do.	1.8 to 2.0	105.4% \pm 4.7	39 to 45	42	Brownish, tinge with fine dark particles suspended in it.	2.0 to 2.2	58.0% \pm 7.4
2	Do.	2.0	96.7% \pm 3.7	48 to 50	49	Do.	2.2 to 2.4	65.0% \pm 1.0

TABLE II
Samples of liquor adrenalinae tartratis

Number of samples tested	Character of the original solution	pH range	Average initial potency with standard deviation	Storage period in months	Average storage period in months	Character of the solution after storage	pH range after storage	Average percentage of loss of potency after storage plus standard deviation
2	Colourless, clear.	2.0	105.0% \pm 5.0	4	4	Colourless, clear	2.0	3.5% \pm 0.4
7	Do.	2.0 to 3.8	100.0% \pm 4.5	5 to 7	6	Do.	2.0 to 4.7	5.1% \pm 1.1
5	Do.	2.0 to 3.8	102.8% \pm 3.4	8 to 10	9	Do.	2.0 to 5.0	10.9% \pm 1.4
5	Do.	2.0 to 2.2	100.0% \pm 0.0	11 to 13	12	Do.	2.0 to 2.2	20.6% \pm 5.0
3	Do.	2.0	92.2% \pm 6.3	14 to 16	15	Light brown, clear.	2.0	33.8% \pm 4.7
7	Do.	1.8 to 2.0	102.0% \pm 3.9	19 to 23	21	Light brown with fine dark particles suspended in it.	2.0 to 2.2	42.9% \pm 10.0
18	Do.	2.0	106.2% \pm 11.6	25 to 29	27	Do.	2.0 to 2.3	55.7% \pm 12.6
13	Do.	1.8 to 2.0	107.8% \pm 8.0	30 to 34	32	Brown with dark particles suspended in it.	2.0 to 2.3	63.7% \pm 7.9
4	Do.	2.0	108.6% \pm 5.6	35 to 37	36	Do.	2.2 to 2.5	65.2% \pm 1.8
8	Do.	2.0	104.8% \pm 5.5	40 to 44	42	Do.	2.0 to 2.4	69.0% \pm 5.7
8	Do.	2.0	106.9% \pm 7.6	46 to 50	48	Do.	2.2 to 2.5	71.6% \pm 2.7

Discussion

The factors underlying this phenomenon of deterioration of adrenaline in liquid preparations have not been fully worked out, though several comments have been offered from time to time. The most important causes recognized as responsible for deterioration of adrenaline are alkalinity of the medium, exposure to light, and bad quality of glass containers. In the series of experiments conducted by us, deterioration as a result of change in the hydrogen-ion concentration can be easily discounted. The quality of the glass bottles supplied were strictly tested by random sampling from amongst the samples according to the B.P. method and found to agree to the

official specifications regarding 'limit of alkalinity'. The pH of the solutions, both before testing and after storage, has been carefully checked and found to lie between 2 and 3 except in two cases where the pH was found to be 4.7 to 5. Exposure to strong light or direct sunlight also was apparently not an important factor, as all these samples were in amber-coloured bottles and were kept away from the sun. The room temperature factor is apparently of some importance. This supposition is strengthened by the fact that a number of 'control' samples from the same batches, kept in the refrigerator for almost identical periods, maintained their potency very much better. This observation has been repeatedly confirmed

even after two years of storage. There are possibly other factors involved which are not yet known. Chemically, the loss of potency can be explained on the assumption that 'adrenochrome' is formed as a result of slow oxidation of adrenaline.

Ganguly and Ghosh (1945) have recently given evidence to indicate that the B.P. adrenaline solution does not remain stable even when sodium bisulphite is added to it, a finding which is in close agreement with ours. Foster *et al.* (1945) however have recently claimed to have prepared an improved solution of adrenaline from adrenaline tartrate, which does not show a loss of potency of over 20 per cent during 5 to 6 years' storage. This work has not yet been confirmed. Unless a more stable preparation of adrenaline is available for medical and surgical use in India, it seems desirable to insist that all liquid preparations of adrenaline be 'dated', in a manner similar to the 'dating' of posterior pituitary extracts, and of vaccines and sera. The 'date' suggested is 10 months to a year from the date of manufacture.

Summary

Systematic investigations on the rate of deterioration of solutions of adrenaline hydrochloride and adrenaline tartrate have been carried out after storage periods varying from four months to approximately four years. It is found that both the liquid preparations deteriorate rather rapidly after the first 10 months from the date of their manufacture. The factors underlying this deterioration are not clearly understood as yet. Adrenaline is an emergency drug of very great importance to medical practice, and any deterioration of potency must be considered to be a matter of grave significance to the patients. Pending the development of an improved solution of adrenaline, it seems desirable that all manufacturers in this country should agree to put a 'date of manufacture' and a 'date of expiry' on the label of their preparations. The 'date of expiry' should preferably be 10 months, but in no case it should exceed one year from the date of manufacture.

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OCULAR MANIFESTATIONS IN MALARIA

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A NUMBER of cases of malaria with ocular manifestations have been noticed by the writers. Though mention of many of these symptoms can be found in the literature, a few of the symptoms seen by us were interesting clinically. External affections of the eye, *e.g.* conjunctival discolorations and herpetic keratitis have been found. Hæmorrhagic conditions of the retina and vitreous, and amblyopia, both due to the disease itself and to quinine, were seen in some cases. A number of cases of cerebral malaria, especially the meningitic and encephalitic forms, showed papillitis of the optic disc, and interesting clinical signs due to the affection of the visual and oculomotor centres and of the vestibular nuclei and their secondary connections. In this paper an attempt is made to classify the conditions encountered; some illustrative case notes are also given.

Manifestations due to the disease itself

In the conjunctiva, marked pallor may be noticed in malarial hæmolytic anæmia. Cases with icteroid discoloration have been seen in the bilious remittent type.

In the cornea, herpex simplex keratitis varying from mild forms to dendritic ulcers have been found in protracted cases of the illness, more often in the convalescent or in the relapsing stage.

In the vitreous and retina, hæmorrhages have been noticed in a few cases. In rare cases, thrombosis of the retinal veins, diffuse retinitis, or retinitis proliferans, as a sequel to retinal hæmorrhages, may be produced, resulting in permanent impairment of vision.

Neurogenic lesions.—The essential pathology of these lesions is obstruction to the vascular supply of the visual and oculomotor centres and of the vestibular nuclei or the region of their secondary connections.

Swelling of the optic disc varying from 1 to 3 diopters, with a marked cherry-red coloration, has been noticed in a number of cases of falciparum malaria, with symptoms of meningitis and coma. In severe cases, the 'choked disc' with exudate and hæmorrhages was seen, with dilated pupils and sluggish or absent reaction to light. Routine antimalarial treatment and lumbar puncture relieved the condition, but one case was left with secondary optic atrophy.

The malarial amblyopia seen is transitory in nature, lasting usually a few hours and causing blindness in one eye with hemianopsia in the other, or blindness in both eyes. Fundus examination does not reveal any abnormality.

Anisocordia or inequality of pupils was also seen. The constriction or dilatation of the pupil in one eye is probably due to the involvement of the pupil dilator or pupil-constrictor centre (accessory small-celled nucleus of Edinger-Westphal), both of which lie in close association with one another in the midbrain.

Convergent strabismus and glycosuria were also noticed. These are due to involvement of the nucleus of Perlia, the central segment of the oculomotor nucleus, situated in the floor of the third ventricle, and concerned with the mechanism of convergence of the eyeballs.

A patient admitted on 24th October, 1945, with sudden weakness in limbs, clouding of consciousness, a marked degree of convergent strabismus and a mild pyrexia. Blood showed M.T. rings and urine a moderate amount of sugar. With antimalarial treatment the strabismus disappeared and urine became clear.

Nystagmus of eccentric fixation associated with effort to move the eyes horizontally on either side was seen.

A patient admitted with temperature, irritability, and horizontal nystagmus. Blood showed M.T. parasites. With treatment, temperature subsided, but nystagmus persisted. After about a week, the patient developed other symptoms of cerebellar lesion, e.g. intention tremor of fingers, tremor of the tongue. Other organic causes were excluded by blood, cerebro-spinal fluid, and lumbar puncture examinations; W.R. and Kahn tests were negative. It is likely that the nystagmus which was latent in character manifested itself with slight exertions of eccentric fixation, being central in origin and resulting from an acute lesion of the primary vestibular nuclei or their secondary connections.

Manifestations due to drugs in course of treatment

Quinine amblyopia or amaurosis has been seen, and is not a very infrequent complication. It is thought to be due to (1) the toxic effect of the drug on the nerve cells of the optic nerve and (2) vasoconstriction due to the effect of quinine on the retinal arteries acting through vascular innervation. It is probable that in the particular case quoted below, the neural lesion was situated in the upper part of the optic chiasma.

A case of M.T. malaria came with defective vision after oral intake of 60 grains of quinine in 48 hours. Complete amaurosis gradually developed, preceded by tinnitus and deafness. Pupils were dilated and fixed. Ophthalmoscopic examination showed complete pallor of both the discs and constriction of retinal arteries, simulating primary optic atrophy. With the stoppage of quinine and with vasodilator measures such as amyl nitrate inhalation, atropine injection, lumbar puncture, and paracentesis at the sclero-corneal junction, vision gradually returned with concentric contraction in the upper half of the visual field. The discs showed a gradual change of colour from pale white to pale red, with partial filling up of retinal arteries with blood. The visual field, though seemed widened to some extent after three weeks, still showed concentric contraction, more marked in the lower half.

Retinal and vitreous hæmorrhages may occur after large doses of quinine in persons with hæmorrhagic diathesis, and may accompany cutaneous hæmorrhages, or bleeding from the intestinal or urinary passages.

Atebrine may produce yellow discoloration of the conjunctiva.

MYXŒDEMA WITH ASCITES

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ASCITES has been noted occasionally in myxœdema. Escamilla Lissier and Shephardson reported a case in 1935 and reviewed fifteen cases. Watson and others reported two cases in 1941. In other cases the clinical picture was like that of nephrosis, and response to thyroid therapy paralleled that first described by Epstein. Up to 1941, twenty-two well-established cases of myxœdema with ascites have been reported; some of them had pleural effusion and two had associated pericardial effusion. Three other cases of isolated pericardial effusion due to myxœdema have been reported. The present case is one associated with ascites only, and the ascites cleared up completely with thyroid therapy alone.

Case report

A Hindu male, aged 45 years, was admitted for generalized anasarca and anæmia of three years' duration. Three years ago, he noticed puffiness of the face which gradually spread to the limbs. The hair had been falling off for one year. There was constipation, weakness and breathlessness on exertion. The voice was not clear; the patient complained of pain in the elbow and knee-joints.

The patient was a fairly well-nourished person, non-vegetarian, and not addicted to alcohol; generalized swelling of the body with puffiness of the face; hair scanty on the scalp and on the outer portion of eyebrows; skin dry; very slight pitting on pressure of the lower extremities; tongue thickened, teeth dirty, pyorrhœa present. Cardiovascular system—pulse regular, 85 per minute, volume and tension good; heart boundaries—3rd rib above half an inch external to the left mid-clavicular line, right side half an inch external to right lateral sternal line; first and second sounds normal in all areas on auscultation. Abdomen distended uniformly; skin dry and rough; umbilicus everted; liver not enlarged, spleen not palpable; fluid thrill present, shifting dullness present on percussion (see figures 1a and 1b, plate X).

Laboratory findings.—The stool and urine showed no abnormality. Blood—hæmoglobin 55 per cent; total r.b.c. 3.2 millions, microcytic and vacuolated, but no nucleated red cells; anisocytosis present; blood pressure 140/100. Teleradiogram of chest showed an asthenic heart, enlarged on both sides, more to the left. B.M.R. — 25.9 per cent.

Treatment.—The patient was put on thyroid extract and iron by mouth. About 12 days later the blood pressure was 130/90 and the B.M.R. — 10.5 per cent. At the end of three weeks' treatment teleradiogram showed considerable improvement in the cardiac tone; the fluid in the abdomen had disappeared, the swelling of the leg was less, and the face cleared up (see figures 2a and 2b; plate X).

Comments.—In this case, repeated examination of the urine failed to show albumin, and the stools any ancylostoma infection. The ascites was not due to heart failure since its cardinal features were absent. The patient was not tapped, and the ascites cleared up with thyroid only.

I am thankful to Rao Bahadur Dr. T. Satakopan and the Superintendent, Government General Hospital Madras, for permission to report this case.

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A Mirror of Hospital Practice

INJURY OF THE PANCREAS AND ITS SEQUELÆ

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THE pancreas is an organ which is deeply situated in the posterior part of the abdomen. It is sometimes injured in 'run-over' accidents or crush injuries. The immediate effects are severe shock due to irritation of the solar plexus, but sooner or later the symptoms of internal hæmorrhage dominate the clinical picture. Associated with the pancreas, the neighbouring organs, the stomach and duodenum also share in the contusion, and the stomach injury may be manifested by blood-stained vomit, as occurred in case 1 described below. Recorded cases show that usually the organ is contused, and, if the pancreatic ferments have free play, acute hæmorrhagic pancreatitis is produced. The part which lies against the vertebral column is most liable to injury. Occasionally the whole organ gets disrupted into two parts, as occurred in case 1, or the tail may get avulsed with the avulsion of the splenic pedicle. The suturing of such friable ruptured pancreatic tissue is difficult. Silk thread may resist absorption by pancreatic enzymes but it may remain as a foreign body and may help in the production of a fistula. Chromicised catgut appears preferable.

There is the likelihood of disturbance of pancreatic secretions as an aftermath of the injury. If the patient escapes initial catastrophe, he may later on get a pancreatic pseudo-cyst. The peritoneal covering of the pancreas is torn or digested by the pancreatic enzymes, and fluid collects in the omental bursa. The boundaries of the bursa limit the extent of the cyst.

Two cases of pancreatic injury are reported below:—

Case 1.—A male, aged 14 years, was admitted on 15th September, 1945, in the Podar Hospital, Bombay, 2 hours after an injury due to a fall of a heavy wooden box on the epigastric region. On admission, his general condition was fair, temperature 97°F., pulse 90, respiration 30. He had practically recovered from the initial shock; the only positive sign was tenderness and rigidity in the upper abdomen. The urine showed no abnormality. By 8 p.m. dullness had appeared in the left hypochondriac region, but no shifting dullness was detected. The pulse rate had risen to 104. He vomited blood four times.

16th September, 1945. Temperature 100.4°F., pulse 118, respiration 34. He had five black-coloured vomits during the night. Slight distension of the abdomen was present and tenderness and rigidity had increased downwards; there was still no shifting dullness.

At 2 p.m. the patient was operated on under ethyl-chloride and ether anaesthesia. The abdomen was opened by an upper right paramedian incision. A large quantity of dark-coloured blood welled out from the peritoneal cavity. There was contusion of the wall of the stomach. Liver and spleen were normal. Through a rent in the lesser omentum more blood poured out. The lesser sac was filled with blood. On mopping out, the peritoneum covering the pancreas was seen torn, and the pancreas was lacerated and ruptured into two parts. The pancreas was sutured with chromicised catgut and a large-sized drainage tube was brought out through the lesser omentum and through the abdominal incision. The abdomen was closed in layers.

In the immediate post-operative period, morphia was given and 250 c.cm. of plasma and 300 c.cm. of saline intravenously.

Two days later he developed crepitations at the base of the right lung, with a high temperature. Penicillin 20,000 units were injected every 3 hours and after 24 hours the condition cleared.

A day later the blood examination revealed a moderate normocytic anaemia, and a marked leucocytosis (18,000, polymorphs 71 per cent). There was no abnormality in the urine. The fasting blood sugar was 154 mg. per cent.

The drainage tube was shortened, and removed one week after operation. There was slight discharge from the track of the drainage tube for a few days. The wound had completely healed and the patient was discharged on 23th October, 1945. He was again seen after a week and the wound was quite healed.

Case 2.—A Sikh, male, aged 25 years, was admitted in the Dayanand Hospital, Ludhiana, with a swelling in the epigastric and left hypochondriac region.

About a month and a half previously while playing football, he received a kick in the abdomen, became unconscious and fell down. He was carried home, and he regained consciousness after a long interval. He started getting pain in the abdomen, and attacks of vomiting; he was constipated, and had had a rise in temperature for a few days. There was no history of jaundice.

On admission the patient looked pale, and the pulse rate was 100. There was a big swelling measuring 10 inches X 8 inches in the epigastric and left hypochondriac regions; it moved with respiration, the lower border was definite and the upper was indefinite. It was dull on percussion, but there was no shifting dullness in the abdomen.

Blood picture: Hæmoglobin 65 per cent; red cells 3.1 million; white cells total 10,000 per c.mm.; polymorphs 78 per cent.

As the count was low, two pints of whole blood was transfused. Next day the patient was operated on under chloroform anaesthesia.

A left upper paramedian incision was made and the abdomen was opened. The stomach presented in front

of the swelling. The incision was enlarged above and below. The swelling was aspirated through the lesser omentum. Fluid came out, and the diagnosis of pancreatic cyst confirmed. The cyst was approached through the lesser omentum above the lesser curvature. The cyst wall was incised, a large drainage tube was placed inside, the fluid was drained, and the wall of the sac was marsupialized. The abdominal incision was closed. Recovery was uneventful.

A CASE OF MADURA FOOT TREATED WITH PENICILLIN

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A HINDU MALE, aged 45 years, of Sarangarh State (E.S.A.), was admitted into the hospital on 21st June, 1945, with swelling of the left foot which was riddled with sinuses, discharging pus and yellow 'sulphur-like' granules; duration 1½ months. The swelling started from the sole and gradually involved the whole foot. The foot was deformed and anatomical landmarks were distorted. It was thickened, considerably swollen and its length was diminished. The foot had an ovoid form, the toes being separated and directed upwards and the sole convex. There was hectic temperature. Smear examination of pus revealed the fungus 'Actinomyces Maduræ', and the case was diagnosed to be one of Madura foot.

Treatment.—Preliminary treatment with sulpha group of drugs and local antiseptic dressing for 7 days produced no improvement.

Multiple radial incisions under anæsthesia followed by daily antiseptic dressing for another 7 days was also of no value.

Penicillin treatment was undertaken under the kind suggestion of Dr. N. G. Ray, chief medical officer, Raigarh State. 10,000 units were given intramuscularly to start with followed by injections of 5,000 units every four hours and a total dose of 100,000 units was given, all intramuscularly.

The temperature came down to normal within 36 hours of the beginning of the penicillin treatment, the pus disappeared in three days and the condition of the wound gradually improved.

The patient was cured and discharged in a month after the administration of penicillin; during the later period of his stay in the hospital only hæmatinic drugs were given with local dressing of the wound.

MENINGOCOCCAL INFECTION COMPLICATING CEREBRAL MALARIA*

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A PATIENT was admitted to hospital at about 10 a.m. in an unconscious state. The history was that he had a high rise of temperature with chill, rigor, and frontal headache, and became unconscious six hours before coming to hospital.

The patient was deeply unconscious and cyanosed. The temperature was 100.6°F., and the blood pressure 120/60. The pulse was of good tension and volume,

and the rate 100 per minute. The heart and lungs were normal; the spleen and liver were not palpable. There was no stiffness of the neck and Kernig's sign was absent. The total white cell count was 6,500 per c.mm. The urine culture was sterile. Examination of the blood showed *P. falciparum* rings.

The patient was treated with intravenous quinine, a total of 20 grains in the day, and 10 grains by Ryle's tube. Continuous oxygen inhalation was given and the patient was fed by Ryle's tube. The temperature came down to 99.4°F. next day and the patient was in a semi-comatose condition. Intravenous quinine was continued. The patient regained consciousness about 36 hours after admission, and after 60 grains of quinine. The urine was tested for quinine and was found positive. Falciparum rings were also seen in thick films.

On the fourth day at about 9-30 a.m. the patient became unconscious again with sudden convulsions, profuse sweating all over the body, rolling of the eyes, frothing of the mouth, and later conjugate deviation of the eyes to the left. No history of epilepsy could be elicited. There were several epileptiform fits that day. The temperature was 101.8°F. and the pulse rate 110; all the tendon reflexes were normal; Kernig's sign negative, only slight restriction of anteroposterior movement of the neck could be detected. Culture of the nasopharyngeal swab showed only colonies of *Streptococcus viridans* and staphylococcus, but no meningococcus. The total and differential white cell counts were within normal limits. Lumbar puncture showed the cerebro-spinal fluid to be quite clear, and under normal pressure; there was no abnormal constituent; a direct smear showed no organism but the culture after 24 hours showed some colonies of meningococcus.

The patient was immediately treated with Dagenan sodium intravenously, and consciousness returned after 12 hours. Later sulphapyridine was given orally.

The case seems to be one of meningococcal infection developing during recovery from an attack of cerebral malaria.

My thanks are due to Drs. A. S. Prowse, R. H. P. Clark, and T. Das for valuable suggestion and help given.

A CASE OF ACUTE MELANCHOLIA TREATED WITH CARDIAZOL AND INSULIN*

By B. L. CHOPRA

Divisional Medical Officer, N.-W. Railway, Ferozepore

A boy, aged 20 years, was admitted to hospital on 1st April, 1945, for the treatment of pain in the neck, back and legs, insomnia and dimness of vision for 20 days, and constipation for 3 days.

The patient was grey-haired, and with prominent eyeballs (exophthalmos) and prominent upper maxillæ. He had a look of depression, and would answer questions very slowly. Tongue dirty and coated; liver and spleen palpable; chest and heart normal; blood pressure 95/65; Kahn test negative; no abnormality in blood and urine; x-ray of the vertebral column normal. The deep reflexes were sluggish, and the plantar reflex was flexor.

(Sedatives did not produce any effect. Purgatives and enema did not improve his constipation. After about a month, he was given cardiazol 6 c.cm. intravenously for three consecutive days. Though no shock or fit was produced, there were some good subsequent effects. The pain all over the body began to diminish. The patient was then given 10 units of insulin half an hour before meals twice daily for 5 days. With this,

*The paper has been condensed. The diagnosis in this case is open to question.—Editor, I.M.G.

all the pains practically disappeared, and the patient was discharged on the 13th May, 1945.

My thanks are due to Dr. C. D. Newman, Chief Medical Officer, N.-W. Railway, for his kind permission to publish this note.

MALARIAL INFECTION IN THE NEW-BORN TRANSMITTED BY MOTHER*

By K. NARAIN RAO, L.M.P.

Assistant Medical Officer of Health, Thondebhavi,
Kolar District, Mysore State

I HAVE read with interest the paper on 'Malarial infection in the new-born' by R. N. Verma, published in the October 1945 issue of the *Indian Medical Gazette*. The following case, which is in a way similar, is much more interesting from the fact that both the mother and child suffered from malaria simultaneously a few hours after delivery.

A Hindu woman, aged 24 years, primipara, gave birth to a male child; the delivery was normal. Next day the mother and child were reported to show shivering movements, but when I attended I found the mother and child quiet though with temperatures of 104.2°F. and 101.6°F. respectively. Information available from the mother and relatives was vague and contradictory. No definite diagnosis was made and palliative treatment was instituted. Forty-eight hours later, the mother had vomiting and nausea and a rigor, and the child was restless, shivering and crying. These symptoms ceased and the temperature of both mother and child rose. The mother showed splenic enlargement, the child did not. Careful enquiry elicited the fact that the mother had been having rigors and fever for a month before delivery. A clinical diagnosis of malaria in mother and child was made and quinine treatment was instituted. There was no more attack of fever. Both responded dramatically to quinine.

A CASE OF LUDWIG'S ANGINA FOLLOWING EPIDEMIC PAROTITIS TREATED WITH SULPHONAMIDE

By SURJYA KUMAR BHOWMICK, L.M.F.

Telepara Tea Estate, Binnaguri, Dooars

THIS severe secondary inflammation as a complication of mumps is a rare occurrence, and the patient's surprising recovery from a rapidly spreading cellulitis under chemotherapy was striking.

The patient, a male, aged 20 years, was admitted to the hospital on 27th October, 1945, with fever, dysphagia, pain and swelling beneath the chin in front of the neck, and stiffness and pain around the jaw.

History.—About a week before, he had fever preceded by chill and rigor, followed by pain, swelling and tenderness below and in front of both ears. He attended the outdoor dispensary; fomentation was given and ichthyol with belladonna and glycerine was painted over the affected parts, for three days. The inflammation subsided but the temperature persisted. On the 26th evening the patient noticed considerable swelling with pain and tenderness beneath the chin

and in front of the neck, and swallowing became difficult.

On admission, temperature 101.2°F.; pulse 118; respiration 20 per minute; redness, swelling and tenderness over the sub-maxillary and sub-lingual regions and in front of the neck, extending to the second intercostal space; gum and teeth healthy; root of tongue, tonsils and fauces slightly congested. That afternoon the temperature rose to 104.8°F., pulse 128, respiration 36 per minute; there was slight dyspnoea; the oedema increased and covered the whole front of the chest and the upper part of the abdomen; and the throat was a little more congested.

Treatment.—The patient was put in Fowler's position and given 5 c.cm. of 10 per cent soluseptasine intravenously. Cold compresses, and pituitrin and adrenalin were given for two days. A course of sulphonamide, 2 tablets every four hours, 4 doses on the first day, 5 doses on the second and 3 doses on the third day was started, followed by one tablet thrice daily for three days. Plenty of glucose water was given.

The next day the general condition improved much; the temperature came down to 97.2°F., pulse 110 and respiration 32 per minute; pain and tenderness were much less and the swelling subsided. Two days later, the temperature was normal, respiration 20, pulse 80 per minute, and the oedema almost subsided.

A CASE OF CHRONIC PEMPHIGUS

By L. M. GHOSH

and

B. K. SEN

(School of Tropical Medicine, Calcutta)

A PATIENT, aged 50 years, had been suffering from chronic pemphigus for about a year when he was an in-patient in this hospital from 19th December, 1944, to 24th January, 1945. He was given treatment consisting mainly of twelve intramuscular injections of calcium and twelve of liver extract, glucose orally and calamine liniment locally, and was discharged apparently cured and free from any blisters. Two months later, he had a relapse and was admitted again on 16th May, 1945, with much more severe symptoms.

On admission.—Mouth septic; temperature 102°F.; pulse weak, 96 per minute; respiration 24 per minute; heart and lungs nothing abnormal; liver and spleen not palpable; the entire cutaneous surface covered with bullae of various sizes, some crusted and some having burst and giving rise to large foul-smelling denuded areas; new eruptions were coming out everywhere including the healed areas.

Nothing particular in family history; clinical and laboratory findings, nothing abnormal.

Treatment.—He was now put on intramuscular injections of penicillin, 5,000 units every four hours up to 100,000 units and 10,000 units every three hours up to 200,000 units, making up a total of 300,000 units; also cardiazol and glucose by mouth. This covered a period of seven days, but did not produce any effect on the skin condition. Sulphathiazole, one gramme thrice daily, with daily injections of calcium and glucose produced no change in the temperature. Pituitrin $\frac{1}{2}$ c.cm. and adrenaline $\frac{1}{2}$ c.cm. for four days were also ineffective. An irregular fever rising to 101°F. continued and new blisters were appearing in crops.

It was then decided to give a course of blood transfusions. The first transfusion was given on 31st May, 1945, but owing to a severe reaction only 30 c.cm. could be given. There were some signs of relief and a general sense of well-being; the patient also became mentally alert, but the temperature persisted. Calcium and glucose were continued.

Two weeks later, due to paucity of blood for transfusion, the patient was given intramuscular injections

* Paper condensed by the editor.

of liver extract, 1 c.cm. twice a week, and sulphadiazine 2 gm. daily for one week. Four days after the commencement of this treatment, the temperature gradually came down to 99°F.

At the second blood transfusion on 21st June, 1945, 300 c.cm. were given, but at the third given five days later, only 150 c.cm. could be given. The patient's general condition improved markedly, the denuded surfaces rapidly healed, and the appearance of fresh blisters was considerably reduced. Calcium and glucose injections were now stopped (after 35 injections). The temperature was normal on 12th July, 1945. At the fourth transfusion given two days later 500 c.cm. were given.

About ten days later, the temperature rose again to 101°F.; sulphadiazine, 2 gm. daily, was started and it subsided.

The fifth transfusion of 300 c.cm. was now given.

After about another ten days, the fever again rose to 101°F. A second course of penicillin, 20,000 units initially followed by 10,000 units every three hours up to a total of 500,000 units was given and the temperature was reduced. Later, a third course of penicillin, 10,000 units every four hours up to 400,000 units was also given.

Subsequently the sixth and seventh transfusions were given 250 and 300 c.cm. respectively. The patient was discharged on 21st September, 1945, about four months after admission, with no eruptions on his body and all the ulcers healed up.

Comments.—Cases of chronic pemphigus show periods of remission entirely independent of any treatment. The assessment of the results of any form of treatment is therefore very difficult. In this case the first attack subsided with little treatment. Regarding the relative value of the different forms of treatment given in the second attack it is difficult to express an opinion. Blood transfusion appears to have some effect and sulphadiazine a little, but there was no definite indication of response to penicillin. Relapses of course are probable.

A CASE OF INGUINAL GRANULOMA (GRANULOMA INGUINALE TROPICUM) IN BENGAL

By L. M. GHOSH

and

D. PANJA

School of Tropical Medicine, Calcutta

(Medical Mycology Enquiry, Indian Research Fund Association)

A BENGALI youth, aged 21 years, was admitted to the Carmichael Hospital for Tropical Diseases for investigation of an ulcer in the groin of four years' duration.

History.—There was a history of exposure four years ago in the Howrah town. There was no penile sore at any time. About a week after the exposure he noticed, on both sides of the groin, small swellings, slightly painful. The swellings were superficial and the pain was not severe enough to interfere with his daily work. After about ten days, the swellings broke down to form small superficial ulcers, one on each side. The ulcers then began to spread laterally in the inguinal region along the folds of the groin. At this time the ulcers became slightly painful and there was a serous discharge. The patient tried various remedies but to no effect. The ulcers on both sides began to

spread further, laterally and medially along the inguinal region, downwards towards the perineum and along the root of the scrotum, encircling the root of the penis on three sides. On the pubic region the two ulcers joined to form a broad ulcerated area.

Examination.—The general health was fairly good, and besides this ulceration he had no other complaints. The ulcer measured on each side about 4 inches long and 1 inch wide. In the middle of the pubic region it was about 2 inches wide and the spread towards the perineum was about 2½ inches downwards on each side. On the left side, the lateral spread was more than on the right. The ulcer was raised above the surface of the skin; the margins were irregular and overhanging the base. The surface looked like granulation tissue and was of a raw beef colour. The discharge was slight, and sero-purulent in nature with an offensive smell. Pain was present but not acute. The patient could not walk but limped with difficulty (see figure in plate X).

Laboratory findings.—Urine analysis—normal. Blood count—normal except a slight increase in polymorphonuclear neutrophils.

Skin reaction to Frei antigen—negative. W.R.—strongly positive.

Smear from the surface scraping showed a marked increase in monocytes which were full of short rod-shaped or oval bodies. (These bodies have been named 'Donovan bodies' but really these are *Klebsiella granulomatis*.)

Culture.—The surface was scraped, and fomentation with normal saline was given every 4 hours for 2 days; after 48 hours, a culture was made from the surface scrapings. Several tubes were inoculated and a pure growth of the organism was thus obtained. The primary culture on glucose-agar media showed small white sticky colonies. Subculture colonies were gelatinous in character, and would trickle down to the bottom of the tube. The organisms were oval or rod-shaped, enclosed in capsules and gram-negative and were identified as *Klebsiella granulomatis*.

Treatment.—As the W.R. was positive the patient was put on arsenic injections first. After three injections of N.A.B. there was no change in the ulcer. The patient was then given bismuth injection (Bismostab) 1 c.cm. intramuscularly once a week. To our utter surprise the ulcer began to heal rapidly. After 3 injections it was stopped for the experimental production of the lesions by inoculation of the culture of *Klebsiella granulomatis*.

Experiments.—Inoculation of the culture and also tissue material failed to produce any lesion in laboratory animals, e.g. guinea-pigs and white rats. An emulsion of the culture inoculated into the patient's thighs one on each side produced granulomatous lesions in a week. The patient absconded from the hospital before the organisms could be recovered from these artificial ulcers.

Although the artificial ulcers were produced by inoculation, the original ulcers went on healing.

Remarks.—The case is reported for the following reasons:

(1) Inguinal granuloma or granuloma inguinale (tropicum) is a tropical disease but its occurrence in Bengal is extremely rare, less than 1 in 20,000 of the skin cases seen here.

(2) The causative organism is the *Klebsiella granulomatis*. It was isolated from the lesions on more than one occasion and an inoculation of the organism produced typical lesions on the patient.

(3) Antimony is said to be the specific drug but in this case bismuth injections were having beneficial effects when the patient absconded from the hospital.



Fig. 1.

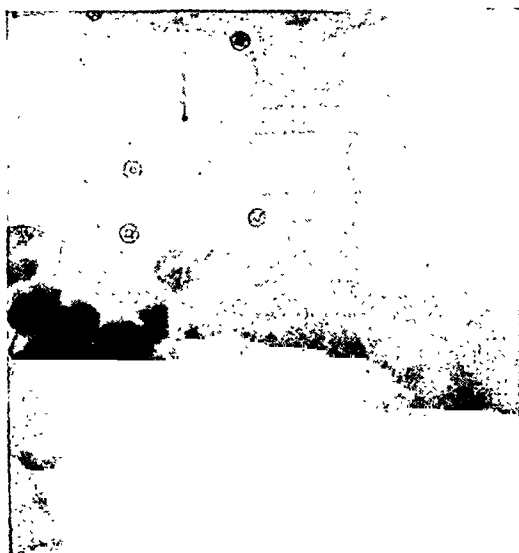


Fig. 2.

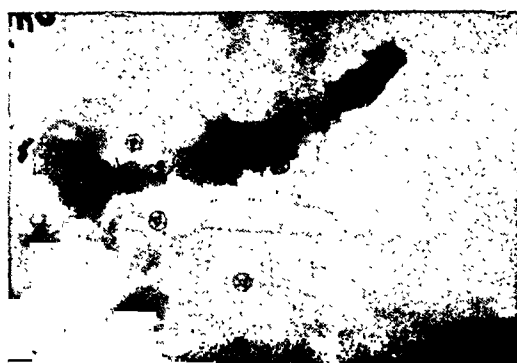
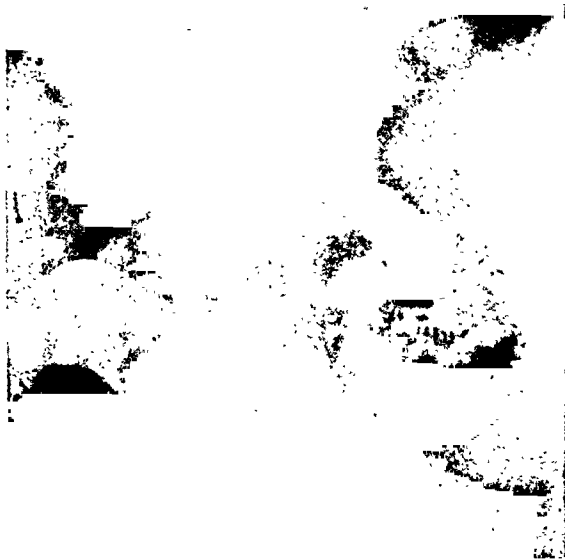


Fig. 3.



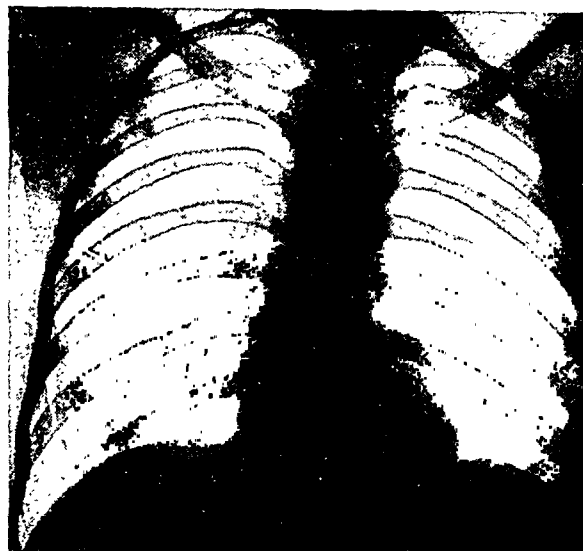


Fig. 1a.—Skiagram showing an opacity in the midzone of the right lung field.



Fig. 1b.—Skiagram after treatment showing complete disappearance of the opacity.

MYXŒDEMA WITH ASCITES ; H. SUBRAMANIAM. PAGE 80.

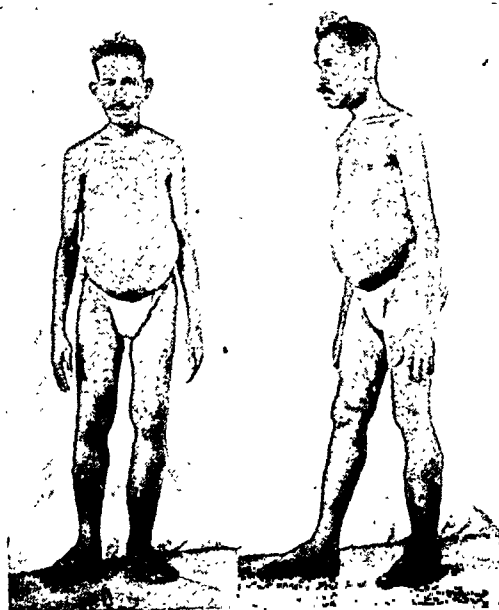


Fig. 1a.

Before treatment.

Fig. 1b.

Front and side views. Anasarca and fluid in the abdomen shown by bulging of the flanks, sparse hair on the scalp.

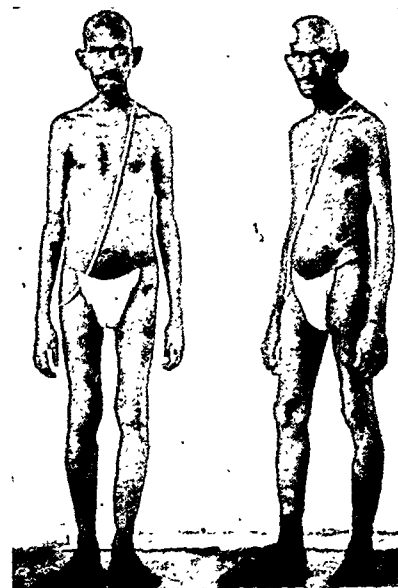


Fig. 2a.

Fig. 2b.

After treatment.

Front and side views.

A CASE OF INGUINAL GRANULOMA
(*GRANULOMA INGUINALE TROPICUM*) IN
BENGAL : L. M. GHOSH & D. PANJA.
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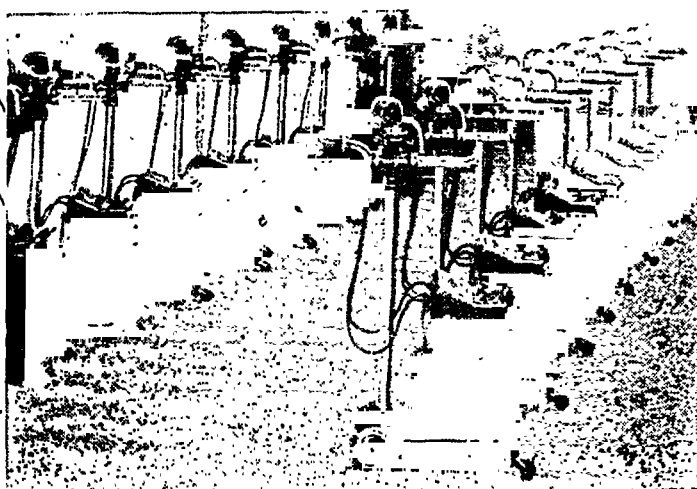
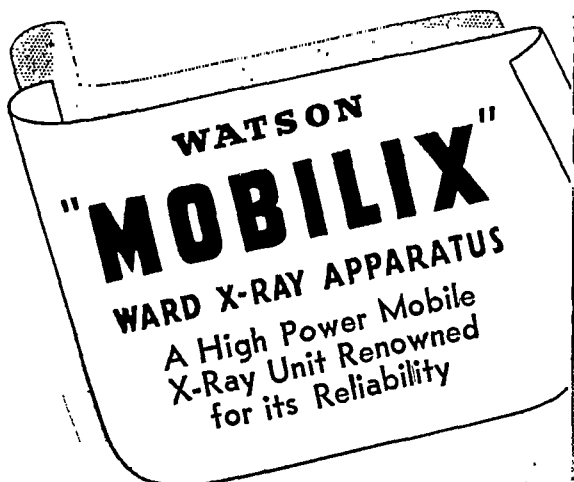
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Indian Medical Gazette

FEBRUARY

INTRAVENOUS ANÆSTHESIA

IN common with other branches of medicine, the practice of anæsthesia has undergone certain important developments during the past decade or so, one of the most important being the introduction of short-acting barbiturates, particularly evipan sodium (hexobarbitone) and pentothal sodium, for intravenous anæsthesia. In comparison with the previously used drugs such as sodium amytal, nembutal and pernocton, these barbiturates quickly produce deep anæsthesia persisting only for a short period and succeeded by rapid recovery of consciousness, and this renders them of particular service for those operations which, although of short duration, require an adequate degree of muscular relaxation. As basal narcotics, they have been much in demand to mitigate pre-operative apprehension; many patients dread an anæsthetic more than the operation itself, and appreciate some form of hypnosis by which they fall asleep in their beds and only reawaken when they are back in bed with the operation done. Like all anæsthetic agents, however, they carry some disadvantages and even dangers, but in skilled hands they give a pleasant induction and a wide margin of safety, for which they deserve to be more widely used in our country than at present.

A knowledge of the action of these drugs is essential if they are to be used intelligently. Anæsthetic agents generally act by exerting a depressant effect on cell metabolism and function, chiefly in the central nervous system for which they have a selective affinity. In contrast to anæsthetics given by inhalation or by the alimentary canal, evipan and pentothal sodium, injected into a vein, have a more direct access to the cells of the nervous system, and hence their action is quicker. Thus in an ordinary fit adult at rest, with a circulation time of thirty to sixty seconds, the injected drug reaches the central nervous system, and begins to produce an effect in that period. Unconsciousness is not produced until a certain concentration in the tissues is reached, and consciousness is not regained until enough of the drug is excreted for the concentration to fall below this level. The drug is rapidly metabolized and rendered inactive by the liver, the oxidized products being excreted by the kidneys. It is the property of rapid detoxication which ensures the safety of the patient, and this again depends on his age and basal metabolic rate, the state of circulation and the speed of the injection. In a young person, according to Minnitt and Gillies (1944),

a dose of one-half gramme of pentothal sodium is usually broken down and detoxicated very rapidly, so that the anæsthetic effect is somewhat short-lived, but in elderly subjects with a low metabolic rate, elimination is much slower and the anæsthesia correspondingly prolonged. When the circulation is sluggish as in shock or over-premedication, there will be a greater time-lag between the commencement of the injection and the onset of anæsthesia; the rate of injection, therefore, must be much slower if a cumulative effect is to be avoided. Then, again, the longer the anæsthesia lasts, the slower is the process of detoxication, when maintenance doses must be given with still greater caution. Finally, pentothal sodium has a somewhat higher potency than evipan (the ratio being approximately 3 : 2) and requires a smaller quantity to produce the same depth of anæsthesia.

Before deciding to administer either of these anæsthetics, it is well to examine the patient and to ascertain if he has suitable veins for injection. He is prepared in the usual way as for other forms of anæsthesia. Although not absolutely essential, premedication by omnopon (gr. $\frac{1}{2}$) and scopolamine (gr. 1/100) about an hour before the administration of anæsthesia, is of value. It enables anæsthesia to be induced and maintained on a smaller quantity of the drug. Everything should be ready before the injection is begun, and the operation should be started immediately unconsciousness is induced, as it is not advisable, except for those with considerable experience, to employ these anæsthetics for surgical procedures lasting more than fifteen to twenty minutes.

It was evipan which made intravenous anæsthesia popular, but it has now been largely replaced by pentothal which, although it causes greater respiratory depression, gives smoother anæsthesia. But one has to be cautious with this drug, for unlike evipan it is irritating to the tissues, and if it gets into the tissues outside the vein, may produce an inflammatory reaction. Again, if it is accidentally introduced into an artery, there will be a burning sensation in the distal part of the limb, and if the injection is not immediately stopped, there will be a risk of arterial obstruction from thrombosis, and possibly gangrene. Such an accident may arise from the presence of an abnormal artery running superficially down the cubital fossa, the normal site of injection, the pulsation of which has been obliterated by a constricting band above the elbow; or the needle may go deep to the cubital vein and enter the brachial artery. The risk is however remote, and need not deter anyone from using pentothal except possibly where no veins are visible; but to be on the safe side, one can observe the colour of the aspirated blood (the crimson of arterial blood is unmistakable) and inject only a minute quantity of pentothal and wait five seconds for any untoward effects before continuing the injection.

A fresh solution of the drug is prepared with distilled water—evipan in 10 per cent and pentothal in 5 per cent strength (both are available in 1 and $\frac{1}{2}$ gramme ampoules), and injected slowly into a convenient vein by means of a record syringe preferably with an eccentric nozzle. The procedure is to give intermittent small doses, the depth of respiration being the guide. At the outset, 0.2 to 0.25 gramme is injected in about fifteen seconds, during which time the patient is encouraged to talk, or asked to count at a slow constant rate. A safety pause is now made for a minute and his reaction to the drug is noted, and if he is still conscious, the injection is continued at the same rate as before, followed by another safety pause. Normally, not more than half a gramme is required to attain a degree of unconsciousness sufficient for his transfer from the bed to the operating theatre and for the induction of the anaesthesia proper. When evipan or pentothal is to be used as sole anaesthetic, the same procedure is followed, *viz.*, the injection of small repeated doses, attention being concentrated on two things—keeping the needle in the vein (alternately the drug can be added from time to time to an intravenous drip of blood, plasma or saline), and watching the patient's respiratory movements. With the onset of unconsciousness, the speech becomes slurred and eventually ceases, the corneal reflexes are lost and the respiration becomes very shallow, but in 15 to 30 seconds it begins to increase again, indicating that the concentration of the drug in the brain has decreased, when a further quantity may be given until an adequate anaesthesia is achieved. Once the patient settles down after induction, further respiratory embarrassment is unusual, and as the operation proceeds, it is only necessary to add small quantities of the drug from time to time to maintain a steady level of anaesthesia. The total dosage varies, depending on the constitution of the patient and the length of the operation, but doses greater than 1.5 grammes are not advised. For longer operations it is usual to discontinue the injection and change over to inhalation anaesthetics.

The chief danger is overdosage, which occurs when a large dose is injected too rapidly or when the injection is continued without regard to the signs of deepening anaesthesia. Rapid respiratory failure may occur and is treated by artificial respiration and oxygen administered under slight pressure in a closed bag. At the same time 2 c.cm. of a 0.3 per cent solution of picrotoxin may be given intravenously. In this form of anaesthesia the lower jaw relaxes readily and tends to obstruct the airway, which is avoided by turning the head to one side with the neck slightly extended, but the jaw needs supporting forwards by an assistant. An oral airway may be inserted, but this should be done gently for fear of provoking laryngeal spasm.

As the barbiturates are broken down in the liver, any gross hepatic disease is a definite

contra-indication to their use. If there is anoxia, it may be aggravated by the respiratory depression produced by the barbiturates; this may be present in fully developed shock, in marked myocardial weakness, or in chronic diseases of the lung such as tuberculosis and emphysema. Respiratory obstruction due to swellings in the neck is particularly dangerous, because of the added risk of laryngeal spasm developing at the time of operation. Toxic patients take a long time to eliminate the drug, and hence are not suitable subjects.

The barbiturates, particularly pentothal sodium, have a wide sphere of usefulness. They allay the patient's nervousness prior to an operation, and as sole anaesthetic agents they are suitable, in the absence of any contra-indications, for practically all minor operations such as orthopaedic manipulation, the reduction of fractures, cystoscopy or urethral dilatation, dilatation and curettage, the extraction of teeth and many other procedures. They are very satisfactory in small fractional doses sufficient to maintain sleep, while an operation is being performed under local, regional or spinal analgesia. Except for the abdominal musculature, relaxation is excellent. The dose needed to produce complete and long-continued relaxation of the abdominal muscles is often large, and apt to cause toxic effects; a change to inhalation anaesthesia is therefore needed in abdominal work. Post-anaesthetic retching and vomiting are rare, and the pulmonary complications are much less common than after inhalation anaesthetics. No costly or cumbersome apparatus is required. But these advantages must not lead one to think that they are quite safe in the hands of a beginner, although all the common pitfalls in administration are readily enough avoided by the experienced anaesthetist.

R. N. C.

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Special Articles

SOME RECENT ADVANCES IN TROPICAL MEDICINE*

By JOHN LOWE, M.D.

School of Tropical Medicine, Calcutta

I HERE attempt to outline briefly some of the contributions to knowledge of tropical disease which have been made during the last few years, and which are either not mentioned or mentioned only briefly in the standard textbooks on the subject. The scope of this discussion is however limited severely. There are many points on

*Read at the annual meeting of the Christian Medical Association held at Nagpur in November 1945.

which it is impossible to touch within the time and space available. Moreover, the matter is discussed mainly from the standpoint of the clinician with chief emphasis on clinical manifestations, diagnosis, and treatment of disease. A few remarks on epidemiology, aetiology and transmission are, however, made.

Even out of the appalling catastrophe of modern war some good can come, and there is no doubt that in medicine, and in tropical medicine in particular, some of the advances has been due to the fact that in the great armies that have been operating in the tropics, tropical disease has been extremely common; so much so that in one theatre of war it was announced that public enemy no. 1 was malaria and public enemy no. 2 was the Japanese. There is no doubt that the armies with their medical staff and their special research units studying specific problems added greatly to our knowledge of tropical disease.

I propose first of all to discuss certain general points arising in connection with numerous tropical diseases and conditions, and then later to discuss certain individual diseases.

General

(a) *Effects of heat.*—A very striking fact is that the old bogey of sunstroke has almost disappeared. The European armies in the tropics have discarded the sola topee and all the paraphernalia and customs previously considered necessary for the avoidance of sunstroke. Heat exhaustion, heat stroke, dehydration, and lack of salt have come to be regarded as responsible for nearly all the morbid conditions caused by the sun, i.e. the sun's heat, and not directly the sun's radiation. An adequate intake of fluids and sodium chloride has come to be regarded as a vital necessity for the prevention of these heat effects, even in healthy persons, and in persons suffering from disease to whom this matter becomes increasingly important. Special steps have been taken in many military hospitals, including the provision of fluid-containers for every bed, with rubber tubes and clamps hanging over the patients so that with a minimum of effort the fluids could be available at any time of the day or night. In severe cases of dehydration, intravenous saline has been given in large amounts with benefit, but some caution is needed to prevent water-logging. For patients who cannot or will not take fluids by the mouth, intra-gastric administration of fluid through a Ryle's tube has been widely adopted, sometimes in the form of continuous drip. In judging the presence or absence of dehydration and the amount of fluid necessary to remedy it, a careful watch on the urine output is important. The output should average at least a pint in four hours. The salt content of the urine can be tested by simple methods, and low values indicate the need for more sodium chloride. Much evidence has been given to show that dehydra-

tion is found in many patients admitted to hospital for many of the common tropical diseases, and that the measures mentioned above have a wide range of applicability.

(b) *Nutrition and deficiency diseases.*—In the conditions associated with war, malnutrition has become increasingly common and there has been considerable growth in our knowledge of vitamin deficiency diseases and their manifestations. It is quite impossible to discuss this matter in any detail here. On the whole in prisoners' camps in various parts of the world the commonest vitamin deficiency condition has apparently been beri-beri. In India, with malnutrition and starvation found in large areas, the rarity of vitamin deficiency diseases was a striking factor. This was particularly so in the Bengal famine. One condition, however, which has attracted considerable attention has been the widespread occurrence of nutritional oedema associated with hypoproteinaemia. Numerous reports on this condition in various parts of the world have been made in recent years, and the clinical manifestations of the condition are now fairly well established. Even in the absence of disease, hypoproteinaemia has been of very common occurrence, and the presence of disease, particularly disease of the gastro-intestinal tract and especially dysenteries, has been an important factor in the production of hypoproteinaemia in many cases. Moreover, nutritional diarrhoea in which vitamin deficiency plays a part and which causes defective absorption of even the food that is available, has been of widespread occurrence, and in many patients have been seen the alternating phases of nutritional diarrhoea and nutritional oedema. Either may develop first; hypoproteinaemia causes oedema which may disappear as the result of the dehydration caused by nutritional diarrhoea; nutritional diarrhoea, when it ceases, is often followed by oedema due to hypoproteinaemia.

It is obvious that the whole question of protein nutrition in health and disease is a matter which needs much more study in this country. Simple methods of doing blood protein estimation are now available, total proteins by the copper sulphate method, and fractions by the biuret method. Moreover, hypoproteinaemia, with or without oedema, is found exceedingly common not only in the general population but in patients admitted to hospital suffering from different diseases, particularly dysentery, malaria, kala-azar, etc. The reduced diet commonly instituted by the patient or his medical adviser in gastro-intestinal disorders in the tropics will frequently induce hypoproteinaemia if it is not already present, and exaggerate it if it is. The whole question of diet in disease in the tropics needs reinvestigation with particular emphasis on this point of protein nutrition. The diet in many hospitals needs revision. Moreover, many tropical diseases damage the digestive organs, particularly the liver, and adequate protein nutrition is a vital necessity in their treatment.

Several methods of remedying hypoproteinæmia have been tried and studied, including oral administration of readily assimilable proteins, if necessary by intra-gastric feeding, the oral administration of proteolysed liver, the intravenous administration of reconstituted blood plasma or blood serum in high concentration, the intravenous administration of protein hydrolysates, etc. On the whole, intravenous medication has been disappointing, and the most generally useful method has been to give good protein diet. In some cases of severe nutritional oedema, mercurial diuretics have proved useful.

(c) *Diagnostic measures*.—Several diagnostic measures have proved of value in the sphere of tropical medicine. Some of these are mentioned under the different diseases, here I may mention a few others. (i) *Lumbar puncture*: During recent years in India conditions associated with cerebral symptoms have been quite common; cerebral malaria, cerebrospinal meningitis and occasionally encephalitis; meningismus is sometimes seen in other diseases such as typhus, typhoid and so on. Lumbar puncture is being increasingly used as a diagnostic measure in investigating these conditions, and also as a therapeutic measure, because even when there is no definite meningitis present the removal of a certain amount of cerebrospinal fluid with reduction in the pressure is frequently of value in relieving cerebral symptoms. (ii) *Sigmoidoscopy*: Sigmoidoscopy has come to occupy a very important place in the investigation of the diarrhoeas and dysenteries and in helping in the isolation of the causal organism. It is of very great value in the study of acute or subacute conditions of the bowel. Its use has been found of value in assessing the results of treatment in individual cases of amebic or bacillary dysentery. Lesions, although of course present elsewhere, will often be visible in the rectum and still more often in the sigmoid. I have heard the opinion expressed that examination of the rectum and sigmoid with a sigmoidoscope should be just as much a routine procedure as the examination of the mouth and tongue in gastro-intestinal disorders. This opinion is perhaps a little extreme, but the great utility of the procedure has been amply confirmed. (iii) *Slide agglutination tests* have recently come to the fore, particularly in the diagnosis of the typhus and typhoid groups of fevers. These tests may be performed almost anywhere with the minimum of laboratory equipment, and various methods of doing the test have been described. The tests are very simple and can be done rapidly and in large numbers. It is stated that agglutination of any diagnostic value can be detected on the slide, and that only if the slide test is positive need the full test be done. It is said that false negatives on the slide do not occur, although false positives are met with. The utility of the test therefore is not in making a definite diagnosis, but in facilitating

laboratory work by greatly reducing the number of complete tests that have to be performed.

(d) *Blood concentration of drugs*.—An important procedure in general medicine which has recently much developed has been the control of medication by the estimation of blood levels of drugs. This has been of importance in the development of treatment with sulphonamides and with penicillin. This measure is now being applied not only in the tropical diseases in which sulphonamides or penicillin administration may be indicated, but also in other diseases such as malaria being treated with mepacrine. Methods have also been evolved for estimating blood mepacrine concentration from the urine concentration. This matter is possibly of considerable importance because it is believed that knowledge of how best to use mepacrine is not yet complete, and in future work a further study of blood levels obtained by different doses will probably be necessary.

(e) *Sulphonamides*.—In the treatment of tropical disease the scope of the use of the *sulphonamide group of drugs* is now becoming more clearly defined. Their great use in tropical medicine is in the treatment of bacillary dysentery, and here they have practically replaced the other forms of treatment, such as saline treatment, bacteriophage treatment, etc. It may be said that the treatment of bacillary dysentery has been completely revolutionized. For some time sulphaguanidine has been considered the drug of choice because of its low absorption rate and the rarity of toxic effects and anuria caused by the deposition of crystals; but recent studies have shown that its absorption must be more than was previously thought, and that anuria from sulphaguanidine can occur. Moreover, several of the other sulphonamides have been shown to be almost if not quite as effective, and sulphathiazole and sulphadiazine are now being widely used for bacterial infection of the intestines.

The only other tropical disease in which sulphonamides are of value because of their direct effect on the causative organism is plague. In this disease, sulphathiazole and sulphadiazine have been reported to give excellent results, and they seem likely to supersede all other forms of treatment. Sulphadiazine is perhaps the drug of choice.

There are, however, numerous other tropical diseases in which the sulphonamides are of great value in combating secondary infections, for example, smallpox, trachoma, secondarily infected amebic conditions, ulcer tropicum, cancrum oris in kala-azar, etc. There are, moreover, some tropical diseases in which the value of the sulphonamides, while suggested, has not yet been fully established. These diseases include cholera, lymphogranuloma inguinale, and the fever of filariasis.

Thus it may be said that the scope of the sulphonamides in tropical medicine is limited although very important. One point I would

mention; the frequency with which in India the sulphonamides are given with a completely inadequate dosage is very striking. Adequate dosage is essential, and on the whole it can be said that in India anuria due to sulphonamides has been extremely rare.

(f) *Penicillin* apparently has a very limited application in the strictly tropical diseases. Its main value in this sphere apparently lies in its effect on the spirochætal organisms and in combating secondary infections. Its use in tropical medicine, however, is at present limited by the fact that most of the spirochætal diseases respond excellently to arsenic, and there is no need to use penicillin. The main exception is Weil's disease in which no specific treatment was previously of value; a small number of cases treated with penicillin has been reported and the results are said to be good.

Penicillin has been reported to give good results in some cases of actinomycosis. It will be interesting to find out of what value penicillin is in the treatment of Madura foot. Penicillin has however been of outstanding value in that very dangerous complication of kala-azar, namely, cancrum oris. Penicillin has given us excellent results in this condition; far better results than those obtained with the sulpha group of drugs. Another condition seen in the tropics in which penicillin may play an important part is ulcus tropicum or Naga sore which has been seen widespread throughout India in recent years. Some recent reports on the treatment of Naga sore with penicillin have been made, and excellent results have been reported. Penicillin may become the treatment of choice; in Naga sore, spirochætes are of course constantly present.

(g) *Transfusion therapy*.—As in other branches of medicine, the scope for transfusion therapy in tropical medicine has widened very considerably. The transfusion fluid may vary very widely according to the pathological condition for which it is used—whole blood, blood plasma, blood serum either fresh or reconstituted after drying; isotonic, hypertonic or hypotonic saline, with or without glucose. All these may have their use in tropical medicine. There is in addition the intravenous transfusion of amino-acids, the results of which on the whole have been however disappointing.

Blood transfusion may be needed in the treatment of the numerous and severe anæmias of the tropics, or of diseases associated with increased red cell destruction or with defective formation of red cells, such as malaria, black-water fever, kala-azar. Saline or glucose saline has a wide range of applicability in cholera, severe dysenteries, dehydration, inanition due to starvation and other conditions associated with peripheral circulatory failure. In some cases the intra-gastric administration of saline has been used instead of intravenous transfusions. For young children particularly, in whom transfusion may be difficult, transfusions into the

bone marrow of the sternum, and in babies into the tibia, may be used.

(h) *Insecticides*.—An important recent advance in tropical medicine has been in the increased knowledge of insecticides and how to use them. I need not discuss here the experiments which demonstrated the great utility of the spray-killing with pyrethrum of adult mosquitoes in houses as an anti-malarial measure; properly done, even in the difficult conditions found in Indian villages, it has been found to lower appreciably the incidence of malaria; the annual cost is quite small. More recently, new insecticides have come into use, DDT and 666. The great value of DDT lies in the fact that it kills both larvæ and adult mosquitoes. Applied to water or to breeding places it destroys all larvæ and stops breeding for several days. Sprayed on walls of houses and huts and the resting places of mosquitoes it kills the mosquitoes which rest there, and the effect may last for several weeks.

I would emphasize that DDT is not a deterrent. The spraying of a single building with DDT will not prevent the occupants of that building being bitten by mosquitoes, although it will greatly reduce the chances of a mosquito surviving long after biting, because the mosquito will usually rest on the sprayed walls. Applied to houses in general in towns or villages, it might reduce the transmission of malaria considerably, although, as I say, it would not prevent mosquitoes coming into the houses. The methods used by the army during the war are probably not practicable by the civil population in peace time; spraying from aeroplanes, the spraying of whole villages and the area round about, are expensive and short-term methods. What we need is a cheap and a longterm policy, and that policy has not yet been worked out. No definite recommendations can yet be made regarding how DDT can best be used to control malaria in the Indian village and countryside. Gammexane (666) is newer and is said to be a more potent insecticide than DDT, but at present little information is available regarding it.

The use of insecticides, however, is not by any means confined to malaria control. Two diseases strike one at once as offering fields for the use of these insecticides, namely, typhus (louse borne) and plague (flea borne). Probably in the future in anti-plague work in India, insecticides will play a considerable part. The spraying of all houses in an area where an outbreak of plague occurs, particularly the floors, might be a valuable anti-plague measure.

A brief mention here might also be made of the deterrents which have been widely used to prevent insect bites during the war by the armies. Dimethyl phthalate (DMP) is possibly the best. Applied to the skin of a person, it will prevent mosquitoes and other insects biting for a considerable period, but the use of this by the

civilian population will probably be very limited.

Malaria

No attempt is made here to deal with the subject of epidemiology, transmission, vectors, etc., about which much detailed information has recently become available. Regarding prevention of malaria also little can be said here. I have already briefly discussed the use of insecticides, pyrethrum, DDT, etc. I will pass on to discuss some other points. One subject at present giving rise to much interest, study and speculation, is the exo-erythrocytic forms of the malaria parasites; the importance of this subject is not merely academic, for it may have a great bearing on treatment.

In spite of the fact that it has very frequently been stated on the authority of Schaudinn that the sporozoites introduced into the body by an infected mosquito enter directly into the red blood cells, various workers have, in the past, postulated that the sporozoites do not do so, but undergo a preliminary phase of development in tissue cells or endothelium before they reach the circulation and enter the red cells. It has long been known, for example, that the blood of a person bitten by an infected mosquito is not infective to another person for several days.

In 1934 the exo-erythrocytic form of the malaria parasite was first demonstrated by various workers in *P. elongatum* of birds, and later in *P. cathemerium*, and the significance of these forms became the subject of much discussion. Later similar forms of *P. gallinaceum* were identified and studied.

There is now developing a general agreement that possibly or probably in all forms of malaria the sporozoites from the mosquito entering the body undergo a phase of development and multiplication in the tissue cells, and this phase is called the tissue, endothelial or exo-erythrocytic phase. From these forms, other forms are given off which enter the red cell and produce the cycle of schizogony. From the cycle of schizogony arise gametocytes which in turn infect the mosquito.

So far this phenomenon has been studied in birds, but it is assumed that a similar development also occurs in man, and in fact one or two workers have claimed to demonstrate it.

The effect of anti-malarial drugs on these exo-erythrocytic or endothelial forms of the parasite has been studied in birds and in tissue culture, and it is found that they are unaffected by quinine and by atebine, but that plasmoquin (in a high, rather toxic, dosage) has some action on them. There is considerable ground for the belief that these forms, and not persistent erythrocytic forms, are responsible for late relapses in malaria; the fact for example that plasmoquin appears to be the only drug which has any action in preventing the sporozoites developing in the human body, and that the administration of plasmoquin possibly or

probably has some effect in reducing relapses. I would however point out that plasmoquin is in any case a toxic drug of limited application, and that the dose of plasmoquin which has to be used to prevent the development of sporozoites and also to make any marked reduction in the relapse rate is dangerously high.

If this work is confirmed in human malaria, it will help to explain many of the anomalous features of human malaria, and will point still more strongly to the outstanding importance of finding a drug which will destroy these exo-erythrocytic forms of the parasite and thus be able to prevent malarial fever developing, if not to prevent malarial infection, and if malaria has developed to reduce markedly the relapse rate. This is possibly the most important line of future development in tropical medicine.

I can briefly mention here only some of the outstanding points about malaria observed in recent years; how the transport of infective persons from one country to another, and possibly the dissemination of mosquito vectors by aeroplanes and other means has created a situation favourable to the widespread occurrence of malaria; the severity of malaria frequently seen in non-immune persons coming to the tropics, or even of immune persons if exposed to infection with new strains of the parasite; the wide range of clinical manifestations of malaria, particularly malaria due to *P. falciparum*, seen in such persons. It is now being more widely realized than ever that the classical malaria with intermittent fever and the 48-hour periodicity and so on is not often seen in the primary attack of malaria in non-immune persons, or in partly immune persons. The 'classical' malaria is really relapsing malaria or malaria seen in people who have had the infection before. In areas where malaria is highly endemic, the importance of regarding every acute fever with almost any type of clinical manifestation as possibly malarial until proved otherwise has been fully realized. Cerebral malaria, algid forms of malaria, and forms of malaria resembling acute dysentery or cholera have occurred widely, also on the other hand the chronic sub-clinical malaria with anæmia and splenomegaly but with no definite history of attacks of fever.

Another point of interest has been the way in which various factors may influence the manifestation of malaria. Malaria has very frequently been found complicating and underlying other conditions, such as heat stroke, heat exhaustion, dysentery, etc. In inanition due to starvation which has been very common during recent years, particularly in Bengal, a heavy malarial infection may produce few or no symptoms, the fever appearing only after the inanition has been remedied. This has been a very important point in the treatment of sick destitutes in Bengal. The manifestations of malaria may also be modified by inefficiently applied and unsuccessful

ful suppressive treatment, which I shall discuss later.

In these circumstances and in the conditions associated with war, the diagnosis of malaria has often presented considerable difficulty, and the demonstration of the parasite has become of greater importance than ever. There has been some discussion as to whether in fever due to malaria it is ever impossible to demonstrate the parasites. Most workers are of the opinion that with careful examination of the thick blood film, repeated if necessary, it is almost always possible to demonstrate the parasite but conditions in the field may often make this impossible.

Rapid methods of demonstrating malaria parasites in blood films have become of great importance, and have been very widely used. Here I would particularly mention the methods of Field which I have used as a routine in recent years, and the method of Simeons which has been used widely in the British army in this country. Both these methods have been published in this journal. Recently another good method was described by Jaswant Singh and Bhattacharji.

A few workers have reported on the value of sternum puncture in demonstrating malaria parasites in difficult cases; other workers have however questioned the utility of the measure.

One fact which has been widely realized has been the great frequency of infection with more than one species of malaria parasites. This is often apparent only with repeated blood examination before, during, or after treatment; in fact in Calcutta in cases studied closely in the School of Tropical Medicine, mixed infections constituted 30 to 40 per cent of the total.

A further point; it has been unsafe in many cases to assume that the mere finding of malaria parasites in the blood gave an adequate explanation of the fever and other symptoms. Malarial infection has been so widespread, and it has very frequently been found complicating other conditions, for example, dysentery and cerebrospinal meningitis. On the other hand the frequency with which malaria due to *P. falciparum* can produce symptoms strongly suggesting other diseases should be borne in mind.

The work on the suppression of malarial fever which was initiated in Malaya before the war has been carried further by army research workers and the *suppressive treatment of malaria* has been of the greatest importance during the war. The drug of choice has been mepacrine (atebrine, quinacrine, etc., are the same thing), and it has been conclusively shown that one tablet taken every day, while it will not prevent malarial infection, will keep that infection at a sub-clinical level for the whole period of administration, and that this effect is still seen even under the intense stresses and strains of active warfare. This measure has been widely adopted by all the allied forces operating in highly malarious areas, and has made possible operations in conditions in which, without this measure, they would have

been quite impossible. The suppressive treatment is continued some time, for many months together, without any appreciable ill effect, and is continued for some little time after the persons have left the malarious area. A large number of persons on cessation of suppressive treatment will develop clinical malaria, which may be sufficiently common to justify mass treatment of every one concerned. After suppressive mepacrine, practically no cases of falciparum infection are encountered, and it has been shown that suppressive mepacrine will not only suppress malarial fever but will cure falciparum infection. These facts are of outstanding importance and interest, although in civilian practice suppressive mepacrine will possibly not be often used.

With supplies of quinine no longer available, *therapeutic treatment* has been based more and more on the synthetic anti-malarials which are identical with the old atebrine. The names mepacrine, quinacrine, etc., are frequently used for the same drug. It has been shown that for the treatment of the ordinary case of malaria mepacrine can entirely replace quinine. Regarding the dosage of mepacrine to be used in the ordinary case the position is not yet quite clear. Before the war and until recently the standard dose in an adult was 0.3 gramme per day for 5 to 7 days. A greater dosage than this and for longer period was considered not devoid of danger, toxic effects sometimes being seen. In the last two years, however, particularly in Europeans and Americans in the army it has been found possible to give considerably larger doses of mepacrine, particularly during the first day or two of the treatment, and this measure has undoubtedly improved the efficacy of the treatment with mepacrine.

The main disadvantage of mepacrine from the point of view of therapeutic effects is the relative slowness of its action. A bigger dose in the beginning of the treatment reduces this disadvantage to some extent. In the army the initial dose on the first day has been 0.8 gramme, a smaller dosage being given on subsequent days, a total of 2.8 grammes being given in 7 days. For civilian use the dosage of 0.4 gramme daily for four days has been recommended. This has the advantage of simplicity but it is not the most effective way of using mepacrine. Possibly a four-day treatment of something like 0.6, 0.4, 0.2, 0.1 gramme would be more effective, slightly more economical and possibly less toxic.

Some mention should be made of the toxic effects of mepacrine. The most important is the condition which has been called mepacrine intoxication, quite a good term because the condition does show some marked similarities to the phase of exaltation due to alcoholic intoxication. It is most commonly seen several days after the institution of mepacrine treatment, and is thus apparently the result of the cumulative effect of mepacrine, the patient being restless, excited, talkative, boastful, and sometimes

developing hallucinations of grandeur and so on. Lack of food and sleep may cause increasing weakness if the condition goes on. The cessation of mepacrine treatment, if it has not already ceased, is imperative, and the use of sedatives and hypnotics may be necessary. Luminal has given good results in my hands. The condition may last only a few hours, but some cases go on for several days, and in a few cases it has persisted for weeks; these cases are possibly those with some inherent mental instability. The incidence of this condition varies rather markedly; the published figures in a large series of cases given therapeutic mepacrine are about 0.4 per cent. The condition does apparently have some relation to dosage, although it may occur even after a relatively small dose such as 1.2 grammes given in 4 days. It seems possible but not certain that the frequency of this toxic effect may be reduced by short courses of mepacrine and by a rapidly diminishing dosage, but more work on the subject is necessary before an opinion can be expressed. This toxic effect of mepacrine is so rare, and usually so evanescent, that it should not be allowed to endanger the general use of mepacrine in malaria. The toxic effects of quinine are perhaps less common but more serious.

One great advantage of mepacrine is its long-continued action. Once a really good therapeutic level has been established in the body, the therapeutic action is maintained over a considerable period of days or even weeks, and mepacrine goes on being excreted for several weeks after the normal therapeutic course; thus the necessity for long courses of mepacrine in the ordinary case is therefore not at all obvious.

In the treatment of the fulminant attacks of malaria, which have been common in recent years, quinine has the advantage of rapidity in action, and in such cases it may be advisable or necessary to give quinine for the first day or two and then revert to mepacrine, or to give quinine and mepacrine for one day and then continue with mepacrine alone. (Thus the slow action of mepacrine can be compensated for.) Intravenous quinine has been widely used, the dosage usually being 6 grains given very slowly at the rate not exceeding 1 grain per minute; and in the severe cerebral malaria these injections can be repeated six-hourly or even four-hourly until the patient is able to take quinine by the mouth. Some remarkable recoveries from fulminating cerebral malaria have been reported under this regime.

Injectable forms of atebriane (mepacrine) were marketed by Bayer before the war, and are now being produced by American and British firms. Bayer's product when injected repeatedly produced mepacrine intoxication too frequently and was definitely dangerous. It is not known whether the new products overcome this difficulty.

And now comes news of a new anti-malarial drug said to be of great potency, M.4888 or paludrine produced by Imperial Chemical

Industries, Manchester. This new paludrine should not be confused with the old paludrine M.3349 which was found effective but perhaps too toxic for general use and has now been abandoned.

Reports of the action of M.4888 have now become available and the researches on which these reports have been based have been most carefully planned and carried out, and the results should be unquestioned.

In the first place the drug acts as a causal prophylactic in falciparum malaria. A person taking the drug in moderate amount if bitten by one or more falciparum-infected mosquitoes does not develop malarial infection since the parasites are destroyed at a very early stage of their development. Such results have not been obtained before with any other drug excepting plasmoquin in a high and toxic dosage. Apparently the drug is not a causal prophylactic of vivax infection, but in small doses, one tablet a day, will suppress fever due to *P. vivax*.

In controlling an attack of malaria, paludrine is extremely effective. It destroys the asexual forms of the parasite. Moreover, the dose needed to control an attack of malarial fever is very small; even one tablet has controlled an attack. Regarding the prevention of relapse it is too early to make any definite statement. In falciparum malaria the relapse so far recorded has been nil, but in this infection the relapse rate is always low. The relapse rate in *P. vivax* infection, even with large doses, appears however to be considerable.

The action of paludrine on the gametocytes in the circulating blood seems to be peculiar in that while it does not cause their disappearance it appears to render them incapable of normal development when ingested by a suitable anopheline mosquito, for such mosquitoes were not found infective to man. Thus paludrine, while undoubtedly being a great advance, is not the solution of the great problem of malaria at the present time, namely relapsing vivax infection.

Other points of importance in the management and treatment of malaria have been emphasized by various workers, such as the use of lumbar puncture in the relief of cerebral symptoms and in the exclusion of possible meningitis, the use of transfusion of saline or glucose saline, serum or plasma or whole blood, in cases with collapse, and the intravenous administration of pentothal sodium in cases of malaria with restlessness, delirium and cerebral manifestations.

The place of other drugs in the treatment of malaria has been studied. Various sulphonamides, particularly sulphadiazine, have been shown to have some action in malaria, but not such as to justify their use in the treatment. Arsenic in the form of neoarsphenamine and mapharside have a marked action on *P. vivax*, but little or no action on *P. falciparum*. Plasmoquin destroys gametocytes and possibly reduces the

relapse rate, but its use has now been largely abandoned because it is the most toxic of all drugs used in malaria.

Relapses, particularly of *P. vivax*, present a great problem in treatment. It is now more fully realized that *P. falciparum* infection rarely produces relapse; recurrence of fever following falciparum infection is usually produced by *P. vivax* which was previously latent. Attempts to reduce the relapse rate by the giving of large doses of mepacrine for long periods have met with little or no success. In a recent group of several hundred such cases studied over a period of one year, the relapse rate after 2.8 grammes mepacrine given in 7 days was still 71 per cent. The problem of malarial relapse is not to be solved by large doses and long administration of quinine, mepacrine or any other drug at present available.

The causation of cerebral manifestations of malaria has been studied in post-mortem material in the army. Blocking of the cerebral capillaries with infected red cells has been reported, and sinus thrombosis has been found in some cases.

Several cases of malaria have been reported of malaria being transmitted by blood transfusion.

The dysenteries

Possibly the greatest advance in tropical medicine has been seen in the treatment of bacillary dysentery with the sulphonamides. The previously used treatments with saline purgatives, bacteriophage and anti-dysenteric serum have now practically died out, although anti-dysenteric serum may still have a place in the treatment of Shiga infection, in addition to, but not instead of, the sulphonamides. The choice of sulphonamides in the treatment of bacillary dysentery has already been discussed; while sulphaguanidine is possibly the best, sulphadiazine and sulphathiazole are perhaps equally efficacious.

In the diagnosis of bacillary dysentery the newer culture media, such as desoxycholate, have proved their value, and the older media are being discarded. The value of sigmoidoscopy in the diagnosis and management of dysentery has already been mentioned.

Amœbic dysentery.—In amœbic dysentery little progress has been made either in aetiology or in treatment, and the subject remains obscure. It is not clear why so many people in countries where amœbic dysentery is not seen are reported to harbour *E. histolytica*. Pathogenic and non-pathogenic strains of *E. histolytica* have been postulated, but have not been proved. The treatment of amœbic infection of the gut remains much in the same position as it was. Emetine can control the symptoms, but often cannot eradicate the infection, and it has been suggested that emetine should only be used to control acute symptoms and then other forms of treatment should be substituted. Various arsenical and iodine preparations have been used in the past and are still used by the mouth, and iodine

preparations as retention enemata. A new iodine preparation, diiodoquin, has been introduced and it is considered to be possibly superior to the old ones. The general feeling is that a new medicament against amœbic dysentery is seriously needed.

The complications of amœbic dysentery have been the subject of numerous publications. The frequency of amœbic granuloma of the gut sometimes wrongly diagnosed as carcinoma should be mentioned. Cases of perforation of the gut have been recorded. Amœbic appendicitis has been reported on numerous occasions, and the inadvisability of operating on the appendix in the possible presence of amœbic infection has been stressed. Liver abscess has been seen in a considerable amount, and the treatment by emetine injections, or emetine plus aspiration, has on the whole been very satisfactory. In secondarily infected liver abscess, penicillin has proved of great value when injected into the abscess cavity. Surgical treatment of liver abscess has been reduced to a minimum.

Cholera

Regarding cholera in recent years little new information has become available. The main subject of work has been the value of sulphonamides in treatment, and different workers have reported different results. It has to be remembered that the main causes of death in cholera are peripheral circulatory failure caused by lack of fluids and salt, and, later, uræmia. If sulphaguanidine does have an effect on the vibrio, it would need to be administered extremely early to make much difference to the prognosis, and the profuse vomiting of the early phases of cholera will often make this difficult or impossible. The vibrios are rapidly eliminated from the body after the acute phase of cholera, and the late administration of sulphaguanidine would appear to be of little value. The main line of treatment in cholera remains the intravenous administration of saline in large amounts. The sulpha group of drugs may be used in addition to this but not instead of it.

Giardiasis

Giardiasis has now become widely recognized as a cause of gastro-intestinal disturbances in children and even in adults, and the value of specific treatment by the administration of atebine has been widely recognized. Some cases however relapse.

The sprue syndrome

Previously it was said that sprue occurred very rarely in Indians. In recent years, however, the widespread occurrence in India of a condition closely allied if not identical with sprue and responding to the same form of treatment has been widely recognized. On the whole, the cases seen are milder than the classical sprue.

Plague

Regarding ordinary bubonic plague, a few points may be mentioned. In recent years the importance of the flea as a reservoir of infection which may be transported from one place to another, or persist for a long period in the same place has been recognized. The infected flea may persist for a long period without feeding, and at the end of the period may infect man, and the importance of measures against the flea as well as against the rat are being more widely recognized. This is where insecticides, such as DDT and 666, may play an important part in anti-plague measures. In the prophylaxis of plague, the value of the attenuated living vaccine rather than the killed plague vaccine has now been widely recognized, and the time may come when it is introduced into India. In the treatment of plague, the sulphonamides have come to occupy an important place, and will possibly supersede all other forms of treatment. Sulphadiazine and sulphathiazole have both given good results, and possibly the first is the best.

Kala-azar

I can only touch briefly on some of the recent advances in kala-azar. The difference in the severity of kala-azar in different countries and peoples has now been recognized, Indian kala-azar being milder than the African. Experimental transmission of kala-azar by infected *P. argentipes* to human volunteers has recently been carried out. There do seem to be certain points about the transmission of kala-azar which are not yet clear.

In the diagnosis of kala-azar, sternum puncture has, to a considerable extent, replaced spleen puncture, since it is practicable much earlier in the disease although it is not quite so reliable. A complement-fixation test using the WKK antigen has been worked out, which gives positive results in kala-azar much earlier than the old aldehyde and antimony tests, etc. These two measures, sternum puncture and the complement-fixation test, have greatly facilitated the early diagnosis of kala-azar.

In treatment, the main advance was the introduction of the aromatic diamidines which however are a little toxic. Diamidino-stilbene (stilbamidine) appears to be the most potent drug in kala-azar, but it is not suitable for the treatment of kala-azar in out-patients, and its use should be reserved for the few antimony-resistant cases, which should if possible be treated in hospital. In the treatment of kala-azar, sodium antimony gluconate which can be given intramuscularly is now being used increasingly. The drug is very rapidly excreted from the body and daily injections are necessary and a high dosage. The immediate results are good, but it is too early to say exactly how many relapse. Relapses appear to be commoner than after urea stilbamine. Intramuscular injections do greatly facilitate the treatment of kala-azar in young children.

Naga sore

A striking fact in 1943 and 1944 was the widespread occurrence in many parts of India of a disease indistinguishable from Naga sore and apparently identical with it. Naga sore was regarded as being confined to certain limited areas in the north-east, particularly Assam, but during this time Naga sore has been reported in Bengal, Bihar, Orissa, Madras, Central Provinces, Ceylon and possibly elsewhere. I need not here describe the clinical manifestations of the condition. Its aetiology is obscure; the constant bacteriological finding in the lesions is the association of the fusiform bacilli with spirochaetes. The treatment of this condition has on the whole been very unsatisfactory, most sores taking several weeks or months to heal. Every physician has his own favourite treatment, which indicates that none is of outstanding value, magnesium sulphate compresses to clean up the sore in the acute sloughing stage, and later mild antiseptics being widely used. In some cases penicillin applied locally and generally has recently been reported to give excellent results, and this may be the treatment of choice in the future.

Tropical eosinophilia

This condition, originally described by Frimodt-Møller and Barton, has now become a widely recognized entity, and thousands of cases have been observed and described in almost every part of India. Cases are also reported from elsewhere, in Ceylon, in the Pacific, and elsewhere in the tropics, and also cases are now being reported in people returned from the tropics to temperate zones, Europe and the United States. The aetiology of this condition remains very obscure, and various theories have been advanced. The treatment with neoarsphenamine has on the whole given very satisfactory results, but it should be noted that the first one or two injections may be accompanied by an increase in the eosinophilia and sometimes in the symptoms, definite improvement appearing later.

Infective hepatitis

This condition, while not really a tropical disease, being seen throughout the world, has been very common in the tropics and subtropics, and some mention should be made of it here. During the war, much study of this condition has been carried out. It has been shown to be caused by a virus which circulates in the blood, and that the disease can be produced in human volunteers by the injection of blood taken during the early stages of the disease. Moreover, it has been shown that many people showing few or no symptoms and no jaundice may have the virus circulating in the blood. The infection has a long incubation period, averaging about 30 days. The mode of transmission is not known for certain. It is considered that some outbreaks have been caused

by the infection of food and water; in other outbreaks, air-borne infection has been postulated, while in still other outbreaks, insect transmission has been suggested. The virus or the group of viruses causing various forms of infective hepatitis are apparently widespread at the present time, and we may mention the epidemic of jaundice after yellow fever inoculation apparently caused by infective human serum used in preparing the vaccine; the outbreaks of jaundice seen in treatment centres for syphilis, jaundice which has been called post-arsenical but which is apparently an infective hepatitis produced by the introduction of the virus into the body of patients from a carrier of the virus, through inadequate sterilization of needles and syringes in clinics. Similar outbreaks of jaundice have been reported in diabetic clinics, through the taking of blood for blood-sugar estimations; and in other circumstances where many injections are given. These findings have focused attention on the methods of sterilizing syringes and needles, and a special report of the Medical Research Council on the subject has just been published. All-glass syringes sterilized by dry heat are recommended, with special precautions to prevent the contamination of syringes. Everyone should obtain and study this report. Needles should be thoroughly cleaned and similarly sterilized. It appears that the use of record syringes, part metal and part glass, makes really adequate sterilization impossible.

Typhus

It has long been known that various forms of typhus were found in India, and some cases had been reported particularly in the army before the war, and also a few civilian cases. During the war, however, thousands of cases of typhus have been seen in the army but only a few civilian cases have been seen. Typhus in the army has been most common in troops undergoing jungle training or in general operations. Cases of typhus have, however, been recorded in considerable number in troops in barracks or in billets even in the suburbs of large cities. Definite outbreaks of typhus have occurred in the suburbs of Calcutta, in a rural area in the Jessore district, in the Ranchi plateau, and elsewhere in India; in Ceylon a large outbreak of typhus involving several hundreds of cases has been seen in troops undergoing training. Typhus has been very common in certain areas of the Assam-Burma frontier in operations against the Japanese, and also in Burma itself. In some areas the number of cases was so great as to endanger military operations, and both American and British armies have established typhus investigation centres and carried out intensive studies of the disease and its transmission. The main findings only can be enumerated here. They have not yet been published in any comprehensive form, though sundry articles on the subject have appeared. The most common form of typhus

in all the areas mentioned has been the form of typhus which is known under the names 'scrub typhus', 'tsutsugamushi' or 'K typhus' because of the typical agglutination of OXK in the Weil-Felix test. Occasionally other forms of typhus have been seen corresponding with murine or flea-borne endemic typhus and a few cases corresponding with the tick borne; but K typhus or tsutsugamushi has been the only one of any importance. In Japan the disease is transmitted by the larval mite *T. akamushi*, a parasite of field rodents, but in Malaya before the war *T. deliensis*, a similar parasite, was considered to be the vector. On the Indo-Burma frontier, *deliensis* has been found infected, and also it is believed other similar parasites of field rodents, but the report on this matter is not yet available. In the South Pacific other Trombiculæ have been found as vectors. The infecting bites are rather anomalously more usually found on the protected parts of the body rather than on the unprotected, and on the body rather than on the limbs. In many cases of scrub typhus, however, particularly those seen in the Calcutta area, no infecting insect bites can be detected. The severity of the disease has varied rather widely in different circumstances, and, in the troops well nourished and well cared for, the mortality has been rather low, usually below 10 per cent and sometimes below 5. I have no space or time here to describe the clinical manifestations of the disease. Actually, the manifestations have varied rather considerably. In the outbreak in and around Calcutta the rash was rather infrequent, the primary scar at the site of an insect bite was practically never seen, the local generalized lymphangitis also was a rare finding, whereas in the cases reported on the Indo-Burma frontier, such manifestations were much more common. The duration of the fever has varied very considerably, some showing the classical 14-day fever, but some showing considerably longer febrile periods and some showing a secondary rise in temperature. Signs in the lungs have been frequently seen, some cases being admitted to hospital under the label of pneumonia. In army practice where typhoid has been practically absent, the diagnosis of typhus is much easier than in civil practice where typhoid is quite common, and the differential diagnosis from typhus in civil practice is often not easy. The Weil Felix often gives negative results until late in the fever, and the diagnostic rise in the XK agglutination may occasionally not appear for sometime after the fever has subsided.

As has been said above, the disease is of sufficient importance in the army to necessitate the appointment of special typhus commissions, and from cases on the Indo-Burma frontier the rickettsiæ have been isolated; and in view of the urgency of the situation research workers abroad have prepared vaccines for this form of typhus which have the power of protecting animals against the infection. The vaccine has only been used to a limited extent in human beings, and

its value as a prophylactic measure has not yet been fully established.

There is little doubt that typhus is much more commonly seen in the civilian population than is at present realized. During the last two months we had no less than 10 definite cases of typhus in Indian civilians in the hospital of the School of Tropical Medicine. One death has been seen. In only two of the cases seen so far has a typical rash appeared, and without thorough investigation the diagnosis of typhoid would usually have been made. We are making it a practice to do the Weil-Felix in every case of undiagnosed fever of more than a few days' duration, and a similar practice adopted elsewhere would probably lead to the discovery of many more cases in civilian population.

The possible value of the slide agglutination test in the diagnosis of typhus has already been mentioned.

The treatment of typhus is on the same lines as the treatment of typhoid. Adequate nursing and adequate nutrition are much the most important. The cerebral manifestations of typhus make nursing and feeding sometimes very difficult. The early appearance of these cerebral manifestations is sometimes a useful point in the differentiation of typhus from typhoid. Many cases however are quite mild, and show practically no cerebral manifestations. It is unlikely that typhus will be found so common as to make immunization against typhus a measure of wide applicability.

Conclusion

These are a few points about some recent advances in our knowledge in the sphere of tropical medicine in India. There are many other points which I might have mentioned. There is much new knowledge now becoming available which will take some time to get into the standard textbooks.

POST-WAR MEDICAL RESETTLEMENT

By K. S. FITCH, O.B.E., F.R.C.S. (Edin.)

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THE immediate post-war period following a modern war brings in its train many complications and difficulties; much planning and thought; not a little heart-burning, worry, and doubt. Though there is no longer danger and destruction; nevertheless, sometimes a new fear is born. What is to happen to me after the war? How shall I find my feet in civil life again? Shall I find employment or shall I have to drag myself from door to door begging for work? These are some of the questions which arise in the minds of service men and women. They look to the State to help them and to start them afresh in life. They are people who are

conscious of a fine job of work done but are also conscious that without careful and sympathetic planning, unemployment and want may be the reward reaped by the defenders of their country.

In India, as in other countries, every effort must be made to avoid unemployment amongst our ex-service men and women. Whilst the Labour Department of the Government of India is vigorously tackling the vast problem of employment for all trades and professions other than that of Medicine and Nursing, the Director-General, Indian Medical Service, has shouldered a similar burden on behalf of our service doctors and nurses.

Medical resettlement organization at the centre.—The Director-General has in his office a separate section whose sole work is medical resettlement, and appendix A sets out the categories of medical and technical personnel in the three services (R.I.N., R.I.A.F., Indian Army and certain members of the R.A.M.C. and R.A.F.) for whom this Resettlement Section is working. The section collects various information concerning service personnel and transfers it on to a card-index system. The information covers those facts and personal records which are likely to be of use in placing individuals into employment. Each card is a short résumé of each individual's qualifications and experience.

Medical resettlement organization in the provinces.—In each province there is now a Medical Employment Bureau, situated in the capital town or city of the province, the address being c/o the Surgeon-General or Inspector-General of Civil Hospitals.

The Provincial Bureau is concerned with the resettlement in the province of ex-service medical men and women of those categories which appear in appendix A. In order to do this resettlement, each bureau has a card-index library containing those cards which have been prepared by the Resettlement Section of the D.-G.'s office in New Delhi. As soon as the cards have been filled in and checked at Delhi, they are sent to the respective provinces.

In most provinces there is a Medical Resettlement Committee, whose concern it is to formulate policy, to interview and select candidates where necessary, and generally to supervise the work of the bureau. These committees are representative, having members drawn from government and from the unofficial medical community. Representatives include those from the administrative, preventive, and nursing branches, as well as non-official representatives of the local graduates and licentiates.

It is the aim and object of the provincial bureaux to find employment for returning doctors, nurses (including nursing orderlies) and medical technicians. Attempts will be made to fit men and women into the type of employment they have asked for in their resettlement *pro formâ*, or for which they apply

to the bureau. There must be obvious limits to this, and not everyone can expect to get the exact appointment he or she would prefer as first choice.

The bureaux cater for employment in government, local board, and private organizations, and also for training as will be explained more fully later in this article.

Medical resettlement in the States.—The general arrangements in the larger States for medical resettlement are similar to those in the provinces, and the following States have instituted Medical Employment Bureaux: Hyderabad, Dholpur, Jaipur, Kotah, Bundi, Cooch Behar and Mayurbhanj.

In some of the larger States where no bureau exists, the chief medical officer carries out the functions of a bureau in his own office.

The case of small States is under consideration at present, but it is possible that they will deal with the nearest provincial bureau.

Medical resettlement into appointments under Government of India, the Railway Board, and in centrally administered areas (Coorg, Ajmer, Delhi Province and Baluchistan).—A Central Bureau has been established as part of the Resettlement Section of the D.-G.'s office in order to deal with the above appointments. This does not mean that separate applications should be made by everyone who wishes to find work under the Government of India or in central areas. Information concerning resettlement wishes already exists in the Resettlement *pro forma* where these have been submitted to D.-G.'s office, but advertisements published by the Federal Public Service Commission calling for applications for certain appointments should be replied to by intending candidates.

Limitation of responsibility of Director-General's office.—This office collects information for distribution to the provincial organizations; it standardizes resettlement methods on a broad basis leaving details for individual provinces to decide according to what is most suited to local conditions; it gives advice on resettlement problems. It does not, however, have any executive power in provincial or State matters nor any direct responsibility in provincial or State resettlement.

The Central Bureau can only put up names of candidates who are *prima facie* suitable for appointments under Government of India, etc., when asked to do so.

It is important to stress the decentralization of medical resettlement responsibility to provinces and States in order that those who have war service to their credit will not be misled into thinking that the D.-G.'s office can appoint them to posts in provinces or States. This misapprehension is not uncommon.

Post-war training

The medical resettlement organization embraces arrangements for post-war training in India of all categories in appendix A; the train-

ing includes post-graduate as well as basic education and also arrangements for licentiates to proceed to the M.B. degree. Again it is provincial or State authorities who will place medical and other similar students and post-graduates into training institutions. Members of the W.A.C.(I.) who wish to get trained as nurses will also be accommodated. The medical and nursing sections of the D.-G.'s office have in mind the requests for training overseas, but it must be clearly stated that very few vacancies will occur in the near future and only a few chosen candidates will be sent overseas either by the Central or by Provincial governments. India can offer facilities for the great majority of trainees either now or within a short time. Medical men and nurses who are contemplating taking privately arranged courses in the United Kingdom should under no circumstances sail from India unless they have received definite offers of vacancies in the British schools and hospitals.

Some miscellaneous information and advice

I. A great number of resettlement *pro forma* pertaining to medical and nursing officers have not yet reached the D.-G.'s office. This delays work and interferes with resettlement.

In the case of V.C.O.'s and other ranks and ratings these *pro forma* will be made out and submitted by the following establishments:—

R.I.N. R.I.N. Record Office, Sewri.

R.I.A.F. R.I.A.F. Headquarters, New Delhi.

Army I.A.M.C.....I.A.M.C. Headquarters, Poona.

Army R.A.M.C.....R.A.M.C. Headquarters, Deolali (where applicable).

Pro forma which are inaccurately completed are of little value.

II. Service orders and instructions dealing with medical resettlement are notified in appendix B.

III. Civil governments are aware of the need to safeguard those who will be released late from the services and will take steps to ensure that there is no differential treatment given to those released early.

IV. From what has been written above it should be evident that when medical personnel of the various categories shown in appendix A return to their homes and require work they must contact the local medical employment bureau. In the case of doctors and nurses a personal visit to the bureau for interview will probably be necessary at some time. Those living near the bureau are advised to make early contact by a personal visit but those living at some distance can write to the bureau in the first place. Nursing orderlies and technicians should approach the civil surgeon of the district as he might himself be able to give employment to the applicant without a further reference to the bureau. Applicants should always take with them any certificates they have showing their qualifications, courses

attended; service discharge certificates and similar papers.

V. The provincial medical authorities are alive to the difficulties of arranging suitable pay for those who have been drawing good pay during the war and who will be employed in provincial medical services. The matter is entirely one for the individual province to decide but no local government is likely to offer pay comparable with army rates. It is not always realized also that the scales of pay in one government department affect, and are affected by, scales in the other departments.

VI. It may not always be possible to offer to each individual exactly the appointment which he or she most desires. This is inevitable and no reasonable offer of employment should be rejected.

VII. In view of the plans for medical reconstruction, both preventive and curative, which are now being drawn up the outlook for medical employment is very hopeful. India is extremely short of doctors and nurses and it is unthinkable that any should be out of work. It may take a certain time, however, to place everyone into his or her right employment.

VIII. There are reliable indications that most service doctors wish to be given government employment. How far this will be possible is not easy to forecast at present but it is unfortunate if these indications mean a revulsion from general private practice. Private practitioners are the backbone of the medical profession in any country. In India they are required in thousands, and inevitably many of our ex-service doctors will have to go into private practice.

These are some of the more important points which should be considered carefully by those who are already released or who will be released later from the Indian services. Civilian readers can assist the work of resettlement by bringing this article to the notice of service relatives and friends.

It will be to India's advantage to give every help possible to returning members of our medical services. They have proved their worth in war and will do so in peace. We must see that they get a fair start again in this great country which is so urgently in need of their professional services. On the other hand, returning service men and women must not expect the impossible and are urged to accommodate themselves to civilian conditions once they are released.

APPENDIX A

CATEGORIES WITH WHICH THE MEDICAL RESETTLEMENT ORGANIZATION IS CONCERNED

Medical and Dental Officers :—

- (1) I.M.S. and I.A.M.C., I.A.D.C., A.I.R.O. (M.), I.T.F.M.C.
- (2) (Licentiates and Graduates) Civil Medical Practitioners.
- (3) Anti-Malarial Medical Officers.
- (4) Recruiting Medical Officers.

- (5) Medical Officers in Ordnance Depots.
- (6) Medical Officers, Provincial Labour Units.
- (7) Medical Officers, Civil Pioneer Force.
- (8) Ships' Surgeons in the Merchant Navy if in service between 3rd September, 1939, and 15th August, 1945.
- (9) Any other category of Medical Officers whose service may hereafter be recognized as War Service 'under Home Department Orders on the subject'.

Nursing personnel :—

- (1) I.M.N.S. (T.).
- (2) A.I.N.S. (R.).
- (3) A.N.S. who desire training or employment as Nurses, Doctors, Health Visitors or Midwives.
- (4) R.I.N. Nurses.
- (5) Male Nurses (Civil Registered).
- (6) Nursing Orderlies who have passed the second grade nursing and Third Class English Examinations :—
 - (A) Specialist Improvers.
 - (B) Mental Nursing Orderlies.
 - (C) Special Treatment Orderlies.
 - (D) Dental Orderlies.
 - (E) Ophthalmic Orderlies.
 - (F) Operating Room Attendants.
 - (G) Sick Berth Attendants, R.I.N.
 - (H) Medical Assistants, R.I.A.F.
- (7) R.A.M.C. Nursing Orderlies of Indian Domicile.
- (8) Demobilized Army personnel including W.A.C. (I.) and W.R.I.N.S. who want training or employment in nursing or allied subjects.

Technicians :—

- (1) Radiographers.
- (2) Laboratory Assistants.
- (3) Dispensers/Compounders.
- (4) Anti-Malaria Assistants.
- (5) Masseurs and Masseuses.
- (6) Warrant Officers, Class II.

APPENDIX B

(a) Indian Army Orders in connection with resettlement of Medical and Nursing Personnel :—

1. General Head-Asks members of I.M.N.S. quarters, India (R.), I.M.N.S. (T.), A.I.N.S. Adjutant General's Branch. (R.) and A.N.S. (I.) to submit their resettlement *pro formæ* to the Director-General, Indian Medical Service.
2. I.A.O. 56/S/45. Describes Labour Department's organization for securing employment for ex-service personnel other than medical.
3. I.A.O. 109/S/45. Describes briefly the Medical Resettlement Organization under Central, Provincial and State Governments.
4. I.A.O. 217/45. Post-war Resettlement I.M.S./I.A.M.C. and I.A.M.C., I.A.D.C. and A.I.R.O. (M.)—Submission to resettlement *pro formæ*.
5. I.A.O. 1206/45. Facilities to members of the A.N.S. for professional training to become fully certificated nurses.
6. I.A.O. 1207/45. Resettlement of civilian doctors on war service.
7. I.A.O. 1208/45. Reminder to all Emergency Commissioned Medical Officers to put in resettlement *pro formæ*. This includes those medical officers who have a civil lien. Points out Units should type their own *pro formæ*.

(b) Indian Army Orders relating to concessions for Service Licentiates desirous of taking M.B. degrees :—

1. I.A.O. 706/44. Concessions for service licentiates who wish to proceed for the M.B. degree.
2. I.A.O. 1286/44. Concessions for I.A.M.C. licentiates desirous of taking M.B. who have passed through the A.M.T.C., Poona.
3. I.A.O. 1959/44. I.A.M.C. licentiates desirous of taking M.B. should notify their names to D.G., I.M.S., and to D.M.S.
4. I.A.O. 1431/45. Concessions for naval licentiates who wish to take M.B. and who have passed the Feroze course.

Medical News

THE SEVENTH SUPPLEMENT TO THE BRITISH PHARMACEUTICAL CODEX

(Abstracted from the *Pharmaceutical Journal*, 17th November, 1945, p. 220)

THIS supplement contains much valuable material. Among the new anaesthetics is *vinyl ether* (venesthene) which is more rapid in action than ether; recovery is said to be more prompt. A new local anaesthetic is *cinchocaine hydrochloride*; its action is similar to cocaine on mucous membranes, and to that of procaine on injection, but is much more prolonged. *Pethidine hydrochloride* has a morphine-like action, though it is more antispasmodic and less narcotic than the opium alkaloid. It is given by mouth or by intramuscular injection, and has produced satisfactory results in the control of labour pains without diminishing the force of uterine contractions.

Amylobarbitone (amytal) is used chiefly as a hypnotic in insomnia and nervous excitability, while its sodium salt is injected when a rapid action is desired. The latter is dissolved in sterilized water, immediately before use. *Pholedrine sulphate* (pholetone, veritol) is useful as a circulatory stimulant and restorative, but is without the cardiac effects of ephedrine. *Dicoumarol*, a principle occurring in spoiled sweet clover, produces a marked prolongation of the prothrombin and coagulation times of the blood.

Of the chemotherapeutic drugs, *propamidine isothionate* is used in the form of a jelly or cream for the prevention and treatment of sepsis in wounds and burns. The action is not inhibited by pus, but *Ps. pyocyanea* infections are unyielding. *Sulphadimethyl-pyridine* (sulphamezathine) may be employed in lobar pneumonia, meningococcal meningitis and in hæmolytic streptococcal infections. The drug is well tolerated and serious toxic effects are infrequent. *Thiouracil* decreases thyroid activity and reduces the basal metabolic rate and is therefore used for thyrotoxicosis, generally in the form of three-grain tablets.

Three new oestrogens are described—*ethistrone*, *hexoestrol*, and *stilboestrol dipropionate*, besides *oestrol* occurring in human pregnancy urine. They are mostly used for ovarian dysfunction and are active by mouth: in males *methyltestosterone* is used orally; it is excreted much more slowly than is testosterone.

The supplement contains 17 monographs on substances included in the last Addendum to the British Pharmacopœia. *Amethocaine hydrochloride* is a local anaesthetic but can also be used for spinal anaesthesia. *Cyclopropane* is a general anaesthetic which is effective in low concentration; induction is smooth and rapid.

Soluble thiopentone (pentothal sodium) and *soluble pentobarbitone* (nembutal) are rapidly acting basal narcotics, the former is useful for short operations, while the latter is most useful in insomnia. *Strophanthin-G* has twice the potency of strophanthin and is excreted more quickly. *Theophylline with ethylenediamine* (cardophyllin) is chiefly indicated for oedema and asthma, having the same action as theophyllin and theophyllin sodium acetate, but is more soluble. *Insulin* and *protamine zinc insulin* can be used side by side to maintain the blood sugar in the diabetic at its proper level. *Dextrose monohydrate*, medicinal glucose or purified glucose is not suitable for administration by injection, but is a frequent component of infants' foods. Among the sulphonamide compounds, soluble sulphacetamide (albuclid soluble) is mainly used for eye infections, sulphadiazine and its sodium salt for general bacterial infections, and soluble sulphapyridine for critically ill patients.

CONTROL OF MALARIA

(Abstracted from the *Medical Bulletin*, Vol. XIV, 10th January, 1946, No. 1, p. 2)

SPEAKING before the Third Bombay Medical Congress Brigadier M. K. Afridi said that of the many advances made in the prevention of malaria in the army, suppressive mepacrine, new repellents and D.D.T. have had a profound and outstanding effect. After giving some detailed accounts he said that the former would be of limited application in civil practice as it could only be employed in a population under strict control. At present the most satisfactory repellent is di-methyl phthalate which may be applied to the skin as a cream, but in the jungle warfare it was found convenient to impregnate nets (ordinary Bengal fish net was found very suitable) with it and wear them as outermost garments close to or touching the skin or clothes. Such impregnated fish nets can be used as sheets for covering the body, but are also of limited application, such as in wealthy households and during railway journeys over malarious regions. The disadvantage of cream is that it has to be repeatedly applied. D.D.T. is notable for its persistent action, the film remaining lethal to insects for days and weeks. Its solution is used by spraying and there are many types of machine for this purpose. In the army it was sprayed from aircrafts extensively where control by ground spraying could not be established in time. Two methods were utilized, viz, 'residual' spraying and 'area' or 'barrier' spraying. The former was employed in static camps where anti-larval control was in force. In this method a film of D.D.T. was deposited once a month on the inner surface of walls and tents. The dosage was one quart of 5 per cent. solution in kerosene oil to 1,000 square feet. The value of the method is still under investigation. In area spraying, the inside and the outside of all buildings, the ground between the buildings and around them to a depth of 50 yards were lightly sprayed at the rate of 5 gallons per acre. Spraying was repeated once a week or fortnight depending upon the entomological reaction. No anti-larval control was attempted except where ponds and pools existed within the circle of area sprayed. The advantage of this method is that it prevents infiltration of mosquitoes whereas with residual spraying such mosquitoes may transmit malarial infection before they are killed by the delayed action of D.D.T. So far evidence shows that it markedly reduced mosquito population, and also the incidence of malaria. With its use malaria control can be extended to rural areas where the existing methods are mostly impracticable, but as finance is a limiting factor in civil practice, the first requirement is to organize cheap production of D.D.T. or to produce a substitute such as benzene hexachloride which is said to be more potent and easier to manufacture.

PHARMACY BILL

By S. H. Y. OULSNAM

(To be introduced in the next session of the Central Legislative Assembly)

RESOLUTION

New Delhi, the 27th November, 1945

No. F. 45-144/45-H(I).—As the compounding and dispensing of medicines by unqualified persons may endanger human life it is necessary to ensure that persons practising the profession of pharmacy have attained a satisfactory standard of education and training. It is accordingly proposed to provide by legislation for the establishment of Pharmacy Councils, for the registration of pharmacists and for the regulation of the education of pharmacists. The Bill for this purpose, which it is proposed to introduce in the next session of the Legislative Assembly, is hereby published for general information.

A

BILL

to regulate the profession of pharmacy

Whereas it is expedient to make better provision for the regulation of the profession of pharmacy and for that purpose to constitute Pharmacy Councils;

It is hereby enacted as follows :—

CHAPTER I

INTRODUCTORY

1. *Short title, extent and commencement.*—(1) This Act may be called the Pharmacy Act, 1945.

(2) It extends to the whole of British India.

(3) It shall come into force at once, but Chapters III, IV and V shall take effect in a particular Province only from such date as the Provincial Government may, by notification in the official Gazette, appoint in this behalf.

2. *Interpretation.*—In this Act, unless there is anything repugnant in the subject or context—

(a) 'agreement' means an agreement entered into under section 20;

(b) 'approved' means approved by the Central Council under section 12 or section 14;

(c) 'British Indian University' means a university in British India established by an Indian law;

(d) 'Central Council' means the Pharmacy Council of India constituted under section 3;

(e) 'Executive Committee' means the Executive Committee of the Central Council or of the Provincial Council, as the context may require;

(f) 'medical practitioner' means a person holding a qualification granted by an authority specified in the Schedule to the Indian Medical Degrees Act, 1916 (VII of 1916) or in the Schedules to the Indian Medical Council Act, 1933 (XXVII of 1933);

(g) 'prescribed' means in Chapter II prescribed by regulations made under section 18, and elsewhere prescribed by rules made under section 45;

(h) 'Provincial Council' means a Provincial Council of Pharmacy constituted under section 19, and includes a Joint Provincial Council of Pharmacy constituted in accordance with an agreement under section 20;

(i) 'register' means a register of pharmacists prepared and maintained under Chapter IV;

(j) 'registered pharmacist' means a person whose name is for the time being entered on the register of the Province in which he is for the time being residing or carrying on his profession or business of pharmacy.

CHAPTER II

THE PHARMACY COUNCIL OF INDIA

3. *Constitution and composition of Central Council.*—The Central Government shall, as soon as may be, constitute a Central Council consisting of the following members, namely :—

(a) six members, among whom there shall at all times be at least one teacher of each of the subjects, pharmaceutical chemistry, pharmacy and pharmacognosy, elected by the authority known as the Inter-University Board from among persons on the teaching staffs of British Indian universities which grant a degree or diploma in pharmacy;

(b) five members, of whom at least three shall at all times be persons possessing a degree or diploma in pharmacy or pharmaceutical chemistry, nominated by the Central Government;

(c) one member elected by the Medical Council of India;

(d) the Director-General, Indian Medical Service, *ex-officio*;

Provided that if he is for any reason unable to be present at a meeting, he may in writing authorize a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote;

(e) the Director of the Central Drugs Laboratory, *ex-officio*;

(f) the Chief Chemist, Central Revenues, *ex-officio*;

(g) one member to represent each Governor's Province elected by the Provincial Council concerned;

Provided that for four years from the first constitution of the Central Council, in the stead of members elected under clause (g), each Government of the Governors' Provinces shall nominate one member, being a person eligible for registration as a pharmacist under section 31.

4. *Incorporation of Central Council.*—The Council constituted under section 3 shall be a body corporate by the name of the Pharmacy Council of India, having perpetual succession and a common seal, with power to acquire and hold property both movable and immovable, and shall by the said name sue and be sued.

5. *President and Vice-President of Central Council.*—

(1) The President and Vice-President of the Central Council shall be elected by the members of the said Council from among themselves;

Provided that for four years from the first constitution of the Central Council the President shall be a person nominated by the Central Government who shall hold office at the pleasure of the Central Government and where he is not already a member, shall be a member of the Central Council in addition to the members referred to in section 3.

(2) An elected President or Vice-President shall hold office as such for a term not exceeding four years and not extending beyond the expiry of his term as member of the Central Council, but subject to his being a member of the Central Council, he shall be eligible for re-election.

6. *Mode of elections.*—Elections under this Chapter shall be conducted in the prescribed manner, and where any dispute arises regarding any such election it shall be referred to the Central Government whose decision shall be final.

7. *Term of office and casual vacancies.*—(1) Subject to the provisions of this section, a nominated or elected member other than a nominated President, shall hold office for a term of four years from the date of his nomination or election or until his successor has been duly nominated or elected, whichever is longer;

Provided that three of the members elected at the first election under clause (a) of section 3, two of the five members first nominated under clause (b) of that section and five of the members elected at the first election under clause (g) of that section (to be chosen in each case by lot under the supervision of the President and in such manner as he may decide) shall hold office for six years or until their respective successors have been duly elected or nominated, whichever is longer.

(2) A nominated or elected member may at any time resign his membership by writing under his hand addressed to the President; and the seat of such member shall thereupon become vacant.

(3) A nominated or elected member shall be deemed to have vacated his seat if he is absent without excuse sufficient in the opinion of the Central Council from three consecutive meetings of the Central Council.

(4) A casual vacancy in the Central Council shall be filled by fresh nomination or election, as the case may be, and the person nominated or elected to fill the vacancy shall hold office only for the remainder of the term for which the member whose place he takes was nominated or elected.

(5) No act by the Central Council shall be called in question on the ground merely of the existence of any vacancy in, or any defect in the constitution of, the Central Council.

(6) Members of the Central Council shall be eligible for renomination or election.

8. *Staff, remuneration and allowance.*—(1) The Central Council may appoint a Secretary who may also, if deemed expedient, act as Treasurer.

(2) The Central Council may, with the previous sanction of the Central Government—

(a) appoint such other officers and servants as may be required to enable the Central Council to carry out its functions under this Act;

(b) fix the salaries and allowances and other conditions of service of the Secretary and other officers and servants;

(c) fix the rates of allowances payable to members of the Central Council.

9. *The Executive Committee.*—(1) The Central Council shall, as soon as may be, constitute an Executive Committee consisting of the President (who shall be Chairman of the Executive Committee) and Vice-President, *ex-officio*, and five other members elected by the Central Council from among its members.

(2) A member of the Executive Committee shall hold office as such until the expiry of his term of office as member of the Central Council, but, subject to his being a member of the Central Council, he shall be eligible for re-election.

(3) In addition to the powers and duties conferred and imposed upon it by this Act the Executive Committee shall exercise and discharge such powers and duties as may be prescribed.

10. *Education Regulations.*—(1) Subject to the provisions of this section, the Central Council may make regulations, to be called the Education Regulations, prescribing the minimum standard of education required for qualification as a pharmacist.

(2) In particular and without prejudice to the generality of the foregoing power, the Education Regulations may prescribe—

(a) the nature and period of study and of practical training to be undertaken before admission to an examination;

(b) the equipment and facilities to be provided for students undergoing approved courses of study;

(c) the subjects of examinations and the standards therein to be attained;

(d) any other conditions of admission to examinations.

(3) Copies of the draft of the Education Regulations and of all subsequent amendments thereof shall be furnished by the Central Council to the Central Government and all Provincial Governments, and the Central Council shall before publishing the Education Regulations or any amendment thereof, as the case may be, take into consideration any comments of the Central Government or any Provincial Government received within three months from the furnishing of the copies as aforesaid.

(4) The Education Regulations shall be published in the official Gazette and in such other manner as the Central Council may direct.

(5) The Executive Committee shall from time to time report to the Central Council on the efficacy of the Education Regulations and may recommend to the Central Council such amendments thereof as it may think fit.

11. *Application of Education Regulations to Provinces.*—At any time after the constitution of the Provincial Council under Chapter III and after consultation with the Provincial Council, the Provincial Government may, by notification in the official Gazette, declare that the Education Regulations shall take effect in the Province:

Provided that where no such declaration has been made, the Education Regulations shall take effect in the Province on the expiry of three years from the date of the constitution of the Provincial Council, unless the Provincial Government, by notification in the official Gazette, postpones such taking effect for such period, not exceeding two years at any one time, as may be specified in the notification.

12. *Approved courses of study and examinations.*—

(1) Any authority in British India which conducts a course of study for pharmacists may apply to the Central Council, where after such inquiry as it may think fit to make, it is satisfied that the said course of study is in conformity with the Education Regulations, shall declare the said course of study to be an approved course of study for the purpose of admission to an approved examination for pharmacists.

(2) Any authority in British India which holds an examination in pharmacy may apply to the Central Council for approval of the examination, and the Central Council, where after such inquiry as it may think fit to make, it is satisfied that the said examination is in conformity with the Education Regulations, shall declare the said examination to be an approved examination for the purpose of qualifying for registration as a pharmacist under this Act.

13. *Withdrawal of Approval.*—(1) Where the Executive Committee reports to the Central Council that an approved course of study or an approved examination does not continue to be in conformity with the Education Regulations, the Central Council shall give notice to the authority concerned of its intention to take into consideration the question of withdrawing the declaration of approval accorded to the course of study or examination, as the case may be, and the said authority may within three months from the receipt of such notice forward to the Central Council through the Provincial Government such representation in the matter as it may wish to make.

(2) After considering any representation which may be received from the authority concerned and any observations thereon which the Provincial Government may think fit to make, the Council may declare that the course of study or the examination shall be deemed to be approved only when completed or passed, as the case may be, before a specified date.

14. *Qualifications granted outside British India.*—The Central Council, if it is satisfied that any qualification in pharmacy granted by an authority outside British India affords a sufficient guarantee of the requisite skill and knowledge, may declare such qualification to be an approved qualification for the purpose of qualifying for registration under this Act, and may for reasons appearing to it sufficient at any time declare that such qualification shall be deemed to be approved only when granted before a specified date.

15. *Mode of declarations.*—All declarations under section 12, section 13 or section 14 shall be made by resolution passed at a meeting of the Central Council, and shall forthwith be published in the official Gazette.

16. *Inspection.*—(1) The Executive Committee may appoint such number of Inspectors as it may deem requisite for the purposes of this Chapter.

(2) An Inspector may—

(a) inspect any institution which provides an approved course of study;

(b) attend at any approved examination;

(c) inspect any institution whose authorities have applied for the approval of its course of study or examination under this Chapter, and attend at any examination of such institution.

(3) An Inspector attending at any examination under sub-section (2) shall not interfere with the conduct of the examination, but he shall report to the Executive

Committee on the sufficiency of every examination he attends and on any other matter in regard to which the Executive Committee may require him to report.

(4) The Executive Committee shall forward a copy of every such report to the authority concerned, and shall also forward a copy together with any comments thereon which the said authority may have made, to the Central Government.

17. *Information to be furnished.*—(1) The Central Council shall furnish copies of its minutes and of the minutes of the Executive Committee and an annual report of its activities together with an abstract of its accounts to the Central Government.

(2) The Central Government may publish in such manner as it may think fit any report, copy or abstract furnished to it under this section or under section 16.

18. *Power to make regulations.*—(1) The Central Council may make regulations consistent with this Act to carry out the purposes of this Chapter.

(2) In particular and without prejudice to the generality of the foregoing power, such regulations may provide for—

(a) the management of the property of the Central Council and the maintenance and audit of its accounts;

(b) the manner in which elections under this Chapter shall be conducted;

(c) the summoning and holding of meetings of the Central Council, the times and places at which such meetings shall be held, the conduct of business thereat and the number of members necessary to constitute a quorum;

(d) the functions of the Executive Committee, the summoning and holding of meetings thereof, the times and places at which such meetings shall be held, and the number of members necessary to constitute a quorum;

(e) the powers and duties of the President and Vice-President;

(f) the tenure of office and the powers and duties of the Secretary, Inspectors and other officers and servants of the Central Council, including the amount and nature of the security to be furnished by the Treasurer.

(3) Until regulations are made by the Central Council under this section, the President may, with the previous sanction of the Central Government, make such regulations under this section, including those to provide for the manner in which the first elections to the Central Council shall be conducted, as may be necessary for carrying into effect the provisions of this Chapter; and any regulations so made may be altered or rescinded by the Central Council in exercise of its powers under this section.

CHAPTER III

PROVINCIAL PHARMACY COUNCILS

19. *Constitution and composition of Provincial Councils.*—Except where a Joint Provincial Council is constituted in accordance with an agreement made under section 20, the Provincial Government shall constitute a Provincial Council consisting of the following members, namely :—

(a) six members, elected from among themselves by registered pharmacists of the Province;

(b) five members, of whom at least two shall at all times be persons possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or members of the pharmaceutical profession, nominated by the Provincial Government;

(c) one member, elected by the Medical Council (by whatever name called) of the Province;

(d) the chief administrative medical officer of the Province, *ex-officio*;

Provided that if he is for any reason unable to be present at a meeting, he may in writing authorize a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote;

(e) the Government Analyst under the Drugs Act, 1940 (XXIII of 1940), *ex-officio*, or where there is

more than one, such one as the Provincial Government may appoint in this behalf;

Provided that where an agreement is made under clause (b) of sub-section (1) of section 20, the agreement may provide that the Provincial Council to serve the needs of the other participating Provinces also shall be augmented by not more than two members, of whom at least one shall at all times be a person possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or a member of the pharmaceutical profession, nominated by the Governments of each of the said other participating Provinces, and where the agreement so provides, the composition of the Provincial Council shall be deemed to be augmented accordingly.

20. *Interprovincial agreements.*—(1) Two or more Provincial Governments may enter into an agreement to be in force for such period and to be subject to renewal for such further periods, if any, as may be specified in the agreement, to provide—

(a) for the constitution of a Joint Provincial Council for all the participating Provinces, or

(b) that the Provincial Council of one Province shall serve the needs of the other participating Provinces.

(2) In addition to such matters as are in this Act specified, an agreement under this section may—

(a) provide for the apportionment between the participating Provinces of the expenditure in connection with the Provincial Council or Joint Provincial Council;

(b) determine which of the participating Provincial Governments shall exercise the several functions of the Provincial Government under this Act, and the references in this Act to the Provincial Government shall be construed accordingly;

(c) provide for consultation between the participating Provincial Governments either generally or with reference to particular matters arising under this Act;

(d) make such incidental and ancillary provisions, not inconsistent with this Act, as may be deemed necessary or expedient for giving effect to the agreement.

(3) An agreement under this section shall be published in the official Gazettes of the participating Provinces.

21. *Composition of Joint Provincial Councils.*—(1) A Joint Provincial Council shall consist of the following members, namely :—

(a) such number of members, being not less than three and not more than five as the agreement shall provide, elected from among themselves by the registered pharmacists of each of the participating Provinces;

(b) such number of members, being not less than two and not more than four as the agreement shall provide, nominated by each participating Provincial Government;

(c) one member elected by the Medical Council (by whatever name called) of each participating Province;

(d) the chief administrative medical officer of each participating Province, *ex-officio*;

Provided that, if any such officer is for any reason unable to be present at a meeting, he may in writing authorize a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote;

(e) the Government Analyst under the Drugs Act, 1940 (XXIII of 1940) of each participating Province, *ex-officio*, or where there is more than one in any such Province, such one as the Provincial Government may appoint in this behalf.

(2) The agreement may provide that within the limits specified in clauses (a) and (b) of sub-section (1), the number of members to be elected or nominated under those clauses may or may not be the same in respect of each participating Province.

(3) Of the members nominated by each Provincial Government under clause (b) of sub-section (1), at least half shall at all times be persons possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or members of the pharmaceutical profession.

22. *Incorporation of Provincial Councils.*—Every Provincial Council shall be a body corporate by such name as may be notified by the Provincial Government in the official Gazette or, in the case of a Joint Provincial Council, as may be determined in the agreement, having perpetual succession and a common seal, with power to acquire or hold property both movable and immovable, and shall by the said name sue and be sued.

23. *President and Vice-President of Provincial Council.*—(1) The President and Vice-President of the Provincial Council shall be elected by the members from among themselves:

Provided that for four years from the first constitution of the Provincial Council the President shall be a person nominated by the Provincial Government who shall hold office at the pleasure of the Provincial Government and where he is not already a member, shall be a member of the Provincial Council in addition to the members referred to in section 19 or section 21, as the case may be.

(2) An elected President or Vice-President shall hold office as such for a term not exceeding four years and not extending beyond the expiry of his term as a member of the Provincial Council, but subject to his being a member of the Provincial Council, he shall be eligible for re-election.

24. *Mode of elections.*—Elections under this Chapter shall be conducted in the prescribed manner, and where any dispute arises regarding any such election, it shall be referred to the Provincial Government whose decision shall be final.

25. *Term of office and casual vacancies.*—(1) Subject to the provisions of this section, a nominated or elected member, other than a nominated President, shall hold office for a term of four years from the date of his nomination or election or until his successor has been duly nominated or elected, whichever is longer.

Provided that three of the members elected at the first election under clause (a) of section 19, two of the members nominated on the first constitution of the Provincial Council under clause (b) of that section, half of the number of members nominated on the first constitution of the Provincial Council under the proviso to the said section, half of the number of members elected at the first election under clause (a) of sub-section (1) of section 21 and half of the number of members nominated on the first constitution of a Joint Provincial Council under clause (b) of that sub-section (to be chosen in each case by lot under the supervision of the President and in such manner as he may decide) shall hold office for six years or until their respective successors have been duly elected or nominated, whichever is longer.

Explanation.—The expression 'half' in the proviso to this sub-section means in relation to an odd number the whole number next below the arithmetical half of such odd number.

(2) A nominated or elected member may at any time resign his membership by writing under his hand addressed to the President, and the seat of such member shall thereupon become vacant.

(3) A nominated or elected member shall be deemed to have vacated his seat if he is absent without excuse sufficient in the opinion of the Provincial Council from three consecutive meetings of the Provincial Council.

(4) A casual vacancy in the Provincial Council shall be filled by fresh nomination or election, as the case may be, and the person nominated or elected to fill the vacancy shall hold office only for the remainder of the term for which the member whose place he takes was nominated or elected.

(5) No act done by the Provincial Council shall be called in question on the ground merely of the existence of any vacancy in, or any defect in the constitution of, the Provincial Council.

(6) Members of the Provincial Council shall be eligible for renomination or re-election.

26. *Staff, remuneration and allowances.*—The Provincial Council may, with the previous sanction of the Provincial Government,—

(a) appoint a Registrar who shall also act as Secretary and, if deemed expedient, Treasurer, of the Provincial Council;

(b) appoint such other officers and servants as may be required to enable the Provincial Council to carry out its functions under this Act;

(c) fix the salaries and allowances and other conditions of service of the Secretary and other officers and servants of the Provincial Council;

(d) fix the rates of allowances payable to members of the Provincial Council.

27. *The Executive Committee.*—(1) The Provincial Council shall, as soon as may be, constitute an Executive Committee consisting of the President (who shall be Chairman of the Executive Committee) and Vice-President, *ex-officio*, and such number of other members elected by the Provincial Council from among themselves as may be prescribed.

(2) A member of the Executive Committee shall hold office as such until the expiry of his term of office as member of the Provincial Council, but, subject to his being a member of the Provincial Council, he shall be eligible for re-election.

(3) In addition to the powers and duties conferred and imposed upon it by this Act, the Executive Committee shall exercise and discharge such powers and duties as may be prescribed.

28. *Information to be furnished.*—(1) The Provincial Council shall furnish such reports, copies of its minutes and of the minutes of the Executive Committee, and abstracts of its accounts to the Provincial Government as the Provincial Government may from time to time require.

(2) The Provincial Government may publish, in such manner as it may think fit, any report, copy, abstract or other information furnished to it under this section.

CHAPTER IV

REGISTRATION OF PHARMACISTS

29. *Preparation and maintenance of register.*—(1) As soon as may be after this Chapter has taken effect in any Province, the Provincial Government shall cause to be prepared in the manner hereinafter provided a register of pharmacists for the Province.

(2) The Provincial Council shall upon its constitution assume the duty of maintaining the register in accordance with the provisions of this Act.

(3) The register shall include the following particulars, namely:—

(a) the full name and residential address of the registered person;

(b) the date of his first admission to the register;

(c) his qualifications for registration;

(d) his professional address, and if he is employed by any person, the name of such person;

(e) such further particulars as may be prescribed.

30. *Preparation of first register.*—(1) For the purpose of preparing the first register, the Provincial Government shall by notification in the official Gazette constitute a Registration Tribunal consisting of three persons, and shall also appoint a Registrar who shall act as Secretary of the Registration Tribunal.

(2) The Provincial Government shall, by the same or like notification, appoint a date on or before which applications for registration, which shall be accompanied by the prescribed fee, shall be made to the Registration Tribunal.

(3) The Registration Tribunal shall examine every application received on or before the appointed date, and if it is satisfied that the applicant is qualified for registration under section 31, shall direct the entry of the name of the applicant on the register.

(4) The first register so prepared shall thereafter be published in such manner as the Provincial Government may direct, and any person aggrieved by a decision of the Registration Tribunal expressed or implied in the register as so published may, within thirty days from the date of such publication, appeal to an authority appointed by the Provincial Government in this behalf by notification in the official Gazette.

(5) The Registrar shall amend the register in accordance with the decisions of the authority appointed under sub-section (4) and shall thereupon issue to every person whose name is entered on the register a certificate of registration in the prescribed form.

(6) Upon the constitution of the Provincial Council, the register shall be given into its custody, and the Provincial Government may direct that all or any specified part of the application fees for registration in the first register shall be paid to the credit of the Provincial Council.

31. *Qualifications for entry on first register.*—A person shall be entitled on payment of the prescribed fee to have his name entered on the first register if he resides, or carries on the business or profession of pharmacy, in the Province and if he—

(a) holds a degree or diploma in pharmacy or pharmaceutical chemistry of a British Indian University or a prescribed qualification granted by an authority outside British India, or

(b) holds a degree of a British Indian University other than a degree in pharmacy or pharmaceutical chemistry, and has been engaged in the compounding of drugs in a hospital or dispensary or other place in which drugs are regularly dispensed on prescriptions of medical practitioners for a total period of not less than three years, or

(c) has passed an examination recognized as adequate by the Provincial Government for compounders or dispensers, or

(d) has been engaged in the compounding of drugs in a hospital or dispensary or other place in which drugs are regularly dispensed on prescriptions of medical practitioners for a total period of not less than five years.

32. *Qualifications for subsequent registration.*—

(1) After the date appointed under sub-section (2) of section 30 and before the Education Regulations have, by or under section 11, taken effect in the Province, a person shall on payment of the prescribed fee be entitled to have his name entered on the register if he resides or carries on the business or profession of pharmacy in the Province and if he—

(a) satisfies the prescribed conditions, or where no conditions have been prescribed, the conditions entitling a person to have his name entered on the first register as set out in section 31, or

(b) is a registered pharmacist in another Province, or

(c) possesses a qualification approved under section 14:

Provided that no person shall be entitled under this sub-section to have his name entered on the register unless he has passed a matriculation examination or an examination prescribed as being equivalent to a matriculation examination.

(2) After the Education Regulations have by or under section 11 taken effect in the Province, a person shall on payment of the prescribed fee be entitled to have his name entered on the register if he has attained the age of twenty-one years, if he resides, or carries on the business or profession of pharmacy, in the Province and if he has passed an approved examination or possesses a qualification approved under section 14.

33. *Scrutiny of applications for registration.*—

(1) After the date appointed under sub-section (2) of section 30, applications for registration shall be addressed to the Registrar of the Provincial Council and shall be accompanied by the prescribed fee.

(2) If upon such application the Registrar is of opinion that the applicant is entitled to have his name entered on the register under the provisions of this Act for the time being applicable, he shall enter the name of the applicant on the register:

Provided that no person whose name has under the provisions of this Act been removed from the register of any Province shall be entitled to have his name entered on the register except with the approval of the Provincial Council recorded at a meeting.

(3) Any person whose application for registration is rejected by the Registrar, may within three months from

the date of such rejection appeal to the Provincial Council, and the decision of the Provincial Council thereon shall be final.

(4) Upon entry on the register of a name under this section, the Registrar shall issue a certificate of registration in the prescribed form.

34. *Renewal fees.*—(1) The Provincial Government may, by notification in the official Gazette, direct that for the retention of a name on the register after the 31st day of December of the year following the year in which the name is first entered on the register, there shall be paid annually to the Provincial Council such renewal fee as may be prescribed and where such direction has been made, such renewal fee shall be due to be paid before the first day of April of the year to which it relates.

(2) Where a renewal fee is not paid before the due date, the Registrar shall remove the name of the defaulter from the register.

Provided that a name so removed may be restored to the register on payment, at any time during the remaining nine months of the year, of double the renewal fee prescribed.

(3) On payment of the renewal fee, the Registrar shall in the prescribed manner endorse the certificate of registration accordingly.

(4) A person whose name is removed from the register under sub-section (2) and not restored thereto under the proviso to that sub-section, shall not be entitled to be again registered except with the approval of the Provincial Council and on such conditions as to payment of fees as it may direct.

35. *Entry of additional qualifications.*—A registered pharmacist shall on payment of the prescribed fee be entitled to have entered in the register any further degrees or diplomas in pharmacy or pharmaceutical chemistry which he may obtain.

36. *Removal from register.*—(1) Subject to the provisions of this section, the Executive Committee may order that the name of a registered pharmacist shall be removed from the register, where it is satisfied, after giving him a reasonable opportunity of being heard and after such further inquiry, if any, as it may think fit to make,—

(i) that his name has been entered on the register in error or on account of misrepresentation or suppression of a material fact, or

(ii) that he has been convicted of any such offence or has been guilty of any such misconduct as in the opinion of the Executive Committee renders him unfit to be a registered pharmacist, or

(iii) that a person employed by him for the purposes of his business of pharmacy has been convicted of any such offence or has been guilty of any such misconduct as would, if such person were a registered pharmacist, render him liable to have his name removed from the register under clause (ii):

Provided that no such order shall be made under clause (iii) unless the Executive Committee is satisfied—

(a) that the offence or misconduct was instigated or connived at by the registered pharmacist, or

(b) that the registered pharmacist has, at any time during the period of twelve months immediately preceding the date on which the offence or misconduct took place, committed a similar offence or been guilty of similar misconduct, or

(c) that any person employed by the registered pharmacist for the purposes of his business of pharmacy has, at any time during the period of twelve months immediately preceding the date on which the offence or misconduct took place, committed a similar offence or been guilty of similar misconduct, and that the registered pharmacist had, or reasonably ought to have had, knowledge of such previous offence or misconduct, or

(d) that where the offence or misconduct continued over a period, the registered pharmacist had, or reasonably ought to have had, knowledge of the continuing offence or misconduct, or

(e) that where the offence is an offence under the Drugs Act, 1940 (XXIII of 1940), the registered pharmacist has not used due diligence in enforcing compliance with the provisions of that Act in his place of business and by persons employed by him.

(2) An order under sub-section (1) may direct that the person whose name is ordered to be removed from the register shall be ineligible for registration in the Province under this Act either permanently or for such period of years as may be specified.

(3) An order under sub-section (1) shall be subject to the confirmation by the Provincial Council and shall not take effect until the expiry of three months from the date of such confirmation.

(4) A person aggrieved by an order under sub-section (1) which has been confirmed by the Provincial Council may, within thirty days from the communication to him of such confirmation, appeal to the Provincial Government, and the order of the Provincial Government upon such appeal shall be final.

(5) A person whose name has been removed from the register under this section or under sub-section (2) of section 34 shall forthwith surrender his certificate of registration to the Registrar, and names so removed shall be published in the official Gazette.

37. *Restoration to register.*—The Executive Committee may at any time for reasons appearing to it sufficient order that upon payment of the prescribed fee the name of a person removed from the register shall be restored thereto.

Provided that where an appeal against such removal has been rejected by the Provincial Government, an order under this section shall not take effect until it has been confirmed by the Provincial Council.

38. *Bar of other jurisdiction.*—No order refusing to enter a name on the register or removing a name from the register shall be called in question otherwise than in the manner provided in this Act.

39. *Issue of duplicate certificates of registration.*—Where it is shown to the satisfaction of the Registrar that a certificate of registration has been lost or destroyed, the Registrar may, on payment of the prescribed fee, issue a duplicate certificate in the prescribed form.

40. *Printing of register.*—As soon as may be after the first day of April in each year, the Registrar shall cause to be printed copies of the register as it stood on the said date, and such copies shall be made available to persons applying therefor on payment of the prescribed charge and shall be evidence that on the said date the persons whose names are entered therein were registered pharmacists.

CHAPTER V

MISCELLANEOUS

41. *Penalty for falsely claiming to be registered.*—(1) If any person whose name is not for the time being entered on the register of the Province falsely pretends that it is so entered or uses in connection with his name or title any words or letters reasonably calculated to suggest that his name is so entered, he shall be punishable with fine which may extend to five hundred rupees:

Provided that it shall be a defence to show that the name of the accused is entered on the register of another Province and that at the time of the alleged offence under this section an application for registration in the Province had been made.

(2) For the purposes of this section—

(a) it shall be immaterial whether or not any person is deceived by such pretence or use as aforesaid;

(b) the use of the description 'pharmacist' shall be deemed to be reasonably calculated to suggest that the user is a person whose name is for the time being entered on the register of the Province;

(c) the onus of proving that the name of a person is for the time being entered on the register of a Province shall be on him who asserts it.

(3) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by order of the Provincial Government or the Executive Committee.

42. *Dispensing by unregistered persons.*—(1) On or after such date as the Provincial Government may by notification in the official Gazette appoint in this behalf, no person other than a registered pharmacist shall compound, prepare, mix, or dispense any medicine on the prescription of a medical practitioner except under the direct and personal supervision of a registered pharmacist:

Provided that this sub-section shall not apply to the dispensing by a medical practitioner of medicine for his own patients, or with the general or special sanction of the Provincial Government, for the patients of another medical practitioner.

(2) Whoever contravenes the provisions of sub-section (1) shall be punishable with simple imprisonment for a term which may extend to six months, or with fine or with both.

(3) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by an order of the Provincial Government.

43. *Failure to surrender certificate of registration.*—

(1) If any person whose name has been removed from the register fails without sufficient cause forthwith to surrender his certificate of registration, he shall be punishable with fine which may extend to fifty rupees.

(2) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by an order of the Executive Committee.

44. *Payment of part of fees to Central Council.*—

The Provincial Council shall before the end of June in each year pay to the Central Council a sum equivalent to one-sixth (or such other proportion as may from time to time be agreed upon by the Central Council and the Provincial Government) of the total fees realized by the Provincial Council under this Act during the period of twelve months ending on the 31st day of March of that year.

45. *Power to make rules.*—(1) The Provincial Government may, by notification in the official Gazette, make rules to carry out the purposes of Chapters III, IV and V.

(2) In particular and without prejudice to the generality of the foregoing power such rules may provide for—

(a) the management of the property of the Provincial Council, and the maintenance and audit of its accounts;

(b) the manner in which elections under Chapter III shall be conducted;

(c) the summoning and holding of meetings of the Provincial Council, the times and places at which such meetings shall be held, the conduct of business thereat and the number of members necessary to form a quorum;

(d) the powers and duties of the President and Vice-President of the Provincial Council;

(e) the constitution and functions of the Executive Committee, the summoning and holding of meetings thereof, the time and places at which such meetings shall be held, and the number of members necessary to constitute a quorum;

(f) the tenure of office and the powers and duties of the Registrar and other officers and servants of the Provincial Council, including the amount and nature of the security to be given by the Treasurer;

(g) the particulars to be stated, and the proof of qualifications to be given, in applications for registration under sub-section (1) of section 32;

(h) the conditions for registration under sub-section (1) of section 32;

(i) fees payable under Chapter IV and the charge for supplying copies of the register;

(j) the form of certificates of registration and the manner of endorsement of renewals thereof;

(k) the maintenance of a register of students in pharmacy;

(l) any other matter which is to be or may be prescribed under Chapters III, IV and V.

FACILITIES TO LICENTIIATE OFFICERS OF THE I.M.S. AND I.A.M.C. FOR ADMISSION TO THE CONJOINT AND OTHER POST-GRADUATE DIPLOMA EXAMINATIONS CONDUCTED JOINTLY BY THE TWO ROYAL COLLEGES

THE Royal College of Physicians of London and the Council of the Royal College of Surgeons of England have approved a recommendation of the Committee of Management of the Examining Board in England to the effect that officers of the I.M.S. or of the I.A.M.C. who are not graduates in medicine and surgery of a university recognized under the regulations of the board and who desire to take the diplomas of the Royal Colleges, may be admissible to the several examinations by means of special facilities granted solely on account of their War Service, as under:—

I. For the diplomas of L.R.C.P., M.R.C.S.

An officer of the I.M.S. or of the I.A.M.C. who produces a personal recommendation from the Director of Medical Services to the effect that he is in every way a suitable candidate, will subject to the production of evidence of his medical qualification be admissible without any further certificates to part I of the First L.R.C.P., M.R.C.S. examination (anatomy and physiology). When he has passed part I he will be required to complete twelve months' clinical work in a recognized general hospital either in this country or overseas, and to pass part II of the first examination (pharmacology and materia medica) before admission to the final examination.

II. For any of the post-graduate diplomas granted jointly by the two Royal Colleges

An officer of the I.M.S. or of the I.A.M.C. who produces a personal recommendation from the Director of Medical Services to the effect that he is in every way a suitable candidate, will subject to the production of evidence of his medical qualification and on complying with the requirements regarding appointments, courses, etc., laid down in the regulations for the several post-graduate diplomas, be admissible to the examinations.

Current Topics

Penicillin Treatment of Early Yaws

By R. R. TOMPSETT

and

G. L. KAUER

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXV, May 1945, p. 275)

FIVE cases of early yaws were treated with penicillin. The drug caused healing of local lesions in all five cases that was comparable to the favourable effect usually obtained with arsenical drugs. In 3 darkfield positive cases the drug caused prompt disappearance of the surface organisms. It is felt that further experimental trial of penicillin is indicated in this disease.

Mode of Action of Penicillin

(Abstracted from the *British Medical Journal*, ii, 6th October, 1945, p. 464)

THOUGH its specificity is rather like that of the sulphonamides, its mode of action is different. For example, it is not antagonized by *p*-aminobenzoic acid, peptones or pus; the sulphonamides are. Further,

penicillin can prevent the growth of sulphonamide-resistant organisms, and the sulphonamides can inhibit the growth of penicillin-fast strains; and whereas the sulphonamides act principally by slowing down the rate of growth, penicillin can cause rapid death and lysis of susceptible micro-organisms.

It is generally held that penicillin has three phases to its action. It may be bacteriostatic, bactericidal, or lytic, according to conditions. Very small amounts, down to one-tenth of the bacteriostatic dose, may cause pronounced morphological changes. Cocci swell to a great size, and bacilli elongate to many times their length. Penicillin is here interfering with the power of the bacteria to divide, and its action would appear to be bacteriostatic.

The assay of penicillin is based on its bacteriostatic action—that is, on the amount which prevents the growth of staphylococci. Sulphonamides help this action, and the presence of even two parts in a million of sulphathiazole markedly increases the apparent titre of penicillin. On the other hand, sulphonamides interfere with its killing and lytic actions. Garrod found that sulphathiazole halved the rate of disinfection of staphylococci by penicillin. This may mean that the 'static' and 'cidal' actions are different, though it seems more logical to assume that they are different degrees of the same action. Bacteriostasis is a loose term, since a stationary population may result from inhibition of growth or from the killing of a fraction of each new generation. The powerful killing and lytic actions are exercised only against dividing bacteria, as Todd, Knox, and Chain and Duthie have demonstrated in investigating the effect of penicillin at different growth phases of the staphylococcus. Chain and Duthie showed that if it is added during the early lag phase the total number of bacteria remains constant for three hours, with a greatly increased turbidity and a decrease in the number of viable organisms. This is due to the production of enlarged forms and to a gradual killing without lysis. If the drug is added at the logarithmic phase of growth when division is rapid it causes a rapid diminution of total and viable bacteria by death and lysis. They found that penicillin becomes effective after a ten-minute lag period, and they assume that this is the time required for one division of the cocci, which having divided are rapidly lysed. When added to an older culture which has reached the stationary phase of growth penicillin does not lyse the culture or affect its respiration. Conditions which increase the rate of division—optimal temperature, use of young cells, or rich medium—all increase the rate of killing and lysis. Conversely, lowering the temperature, dilution of the medium, or presence of growth inhibitors like sulphonamides or boric acid or helvolic acid decrease the killing power.

Penicillin-resistant bacteria are important in considering the mode of action. First, there are the naturally resistant species of bacteria, such as the anaerobic spore bearers, which owe their resistance to their possession of penicillinase, an enzyme which destroys penicillin. A small proportion of the normally sensitive species—for example, staphylococci—are also resistant and also secrete penicillinase. The power of the bacteria to divide is an important factor in resistance; because any strain with an impaired power of division will be classed as penicillin-resistant. Resistant strains may be obtained by subculturing sensitive organisms in broth containing penicillin. The resistant strain so obtained has lost its virulence; it is more easily killed by the body mechanisms; it grows very much more slowly than the parent strain, and it does not secrete penicillinase. It can withstand up to 3,000 times the concentration of drug tolerated by the parent strain. The resistance is only temporary, and after a few cultures in drug-free broth it becomes sensitive and recovers its normal rapidity of growth. This 'reverted' form has a slight residual resistance, up to ten times that of the original culture. The ability of these strains to withstand such high concentrations may not be entirely due to a specific penicillin resistance, but to their greatly reduced growth rate. This view gains

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some support from Demerec's statistical demonstration that such resistance is not brought about by the action of the penicillin, but that the resistant forms arise as a chance mutation and are selected by the drug. Another type of penicillin-resistant staphylococcus is seen in the minute colonies which appear in the otherwise clear zones produced by penicillin in the ring test; these grew slowly, and quickly reverted to a sensitive form on subculturing in normal broth. Other resistant strains are produced by the action of barium chloride on bacteria. This salt is known to destroy or inhibit enzymes, and the resistance of these variants is due to their lowered metabolic activity and slow growth.

It is stated that, unlike the strains made resistant *in vitro*, those obtained during treatment of animals and patients with penicillin are permanently resistant. This statement needs modification before it can be accepted. Schmidt and Sesler claimed to have made a strain of staphylococcus permanently resistant in animals, but it had only four times the resistance of the original culture. Anderson and others isolated resistant strains of staphylococcus from five patients after one week's treatment with penicillin, having shown that the original strains were sensitive. These resistant strains had sixty times the penicillin tolerance of the original strain, and the authors adduced some evidence that the resistance was permanent. The degree of resistance obtained by treatment in animals and patients is of the same order as the residual resistances of the 'reverted' forms from the strains made resistant *in vitro*. It may be that much of the very high resistance obtained *in vitro* is due to non-specific effects on growth, and that the residual resistances obtained after reversion are a true measure of the specific permanent resistance of the strain. Such an effect on growth has been observed, and results in the formation of 'persisters', which, having temporarily lost the power to divide, were not killed by penicillin. These, on being placed into fresh broth, grew normally and were easily killed by the drug.

Very little is known of the mode of action of penicillin. It is inactivated by cysteine, but this appears to be by chemical action on the penicillin and not by interference with its mode of action. Nevertheless, it has been suggested that penicillin may act by interfering with the utilization of thiol groups, by the growing cell. It may interfere with an essential enzyme system in bacteria. It seems, however, to play a more positive part than a mere interference with growth. It may itself form part of an enzyme system and usurp the functions of the normal bacterial enzyme. The fact that penicillin lyses only dividing cells is an important clue. The cell may become susceptible only at the time of division, or penicillin may become activated by bacterial substances produced at that time, or the cell may kill itself by its own products at the time it divides. It is difficult to absolve the cell from the charge of collaboration in its own death.

Reviews

A TEXTBOOK OF SURGICAL PATHOLOGY.—By Charles F. W. Illingworth, M.D., Ch.M., F.R.C.S. (Edin.), and Bruce M. Dick, M.B., F.R.C.S. (Edin.). Fifth Edition. 1945. J. and A. Churchill Limited, London. Pp. viii plus 728, with 306 illustrations. Price, 42s.

THE authors state in the preface that 'this book has been written for graduates and senior students, with the object of providing an account of the pathology of surgical diseases, and especially of those aspects that are outside the scope of textbooks of general pathology'. They have carried out this object in 33 carefully proportioned chapters, well written and well illustrated. The largest chapter (88 pages) is on diseases of bones; the chapter on diseases of the female generative organs

occupies 57 pages, the one on tumours 54 pages, and that on urinary organs 46 pages. The four chapters on diseases of the thorax, skull and brain, stomach and duodenum, and gall-bladder, liver and bile ducts occupy 30 to 40 pages each, while those on breast, mouth, jaws, salivary glands and neck, blood vessels, and male generative organs occupy 20 to 30 pages each. Of the remaining 21 chapters, those on inflammation, wound infections, tuberculosis, and on diseases of joints, muscles, tendon-sheaths and bursae, lymph glands and vessels, spine and spinal cord, peripheral nerves, thyroid gland, pharynx, larynx and oesophagus, small intestine, colon, vermiform appendix, peritoneum and of the pancreas occupy 10 to 20 pages each. Less than 10 pages each are devoted to the chapters on constitutional effects of injury, actinomycosis, hydatid disease, and diseases of the spleen, parathyroid and adrenal glands. In the present edition, the sections on surgical shock and burns, and on anaerobic wound infections have been revised in the light of recent experience, and new subjects, e.g. the crush syndrome, sarcoidosis of Boeck, solitary plasmacytoma of bone, adenolymphoma of the salivary glands, argentaffine tumours of the intestine, and interstitial-cell tumour of the testis have been included.

A book to be highly recommended.

AMPUTATIONS AND ARTIFICIAL LIMBS.—By R. D. Langdale-Kelham, M.R.C.S., L.R.C.P., and George Perkins, M.C., F.R.C.S. 1942. Oxford University Press. Pp. 96, with 39 illustrations

THE EAR, NOSE AND THROAT IN THE SERVICES.—By R. Scott Stevenson, M.D., F.R.C.S.E. 1943. Oxford University Press. Pp. xii plus 116, with 16 illustrations

THE Oxford University Press have planned to bring out a series of war manuals under the general editorship of Lord Horder with a view to documenting adequately the progress in medicine and surgery made as a result of the war. The two books under review belong to this series.

In 'Amputations and artificial limbs', the authors state that they 'have attempted to epitomize the modern views on amputations, leaving out nothing of importance while rejecting all that is superfluous'. The different aspects of amputation are dealt with in seven sections, while the fitting of artificial limbs is described in four sections. For illustrative purposes diagrams instead of photographs have been used, owing to the scarcity of high quality paper, but the diagrams are quite apt for the purpose.

In the first introductory chapter of 'The ear, nose and throat in the services' the importance of accurate recognition and treatment of affections of these organs from the Service point of view are pointed out, and the author states that 'it is not without justification, too, that the claim has been made on behalf of otologists that the proportion of men whose categories are raised after treatment in an ear, nose and throat department is higher than in any other department of a military general hospital'. The six other chapters deal with diseases of the ear and their treatment, two more with those of nose and throat, one with those of the nose and nasal sinuses, and one with those of the pharynx and larynx. New instruments recently invented for helping in the diagnosis of these cases are described. The illustrations given, though not too many, are apt and good.

THE PERMEABILITY OF NATURAL MEMBRANES.—By Hugh Davson, D.Sc., and J. F. Danielli, D.Sc., A.I.C. 1943. Cambridge University Press, Cambridge. Pp. x plus 361, with 73 figures. Price, 25s. net

THESE two experienced research workers attempt in this book to give a general survey of the field of permeability of natural membranes, clearing up the many errors which have crept into the literature. The subject of monolayers is omitted in view of the excellent books available on the subject.

There are twenty-one chapters: Introductory and preliminary topics such as significance of permeability studies, methods of study, equations used, interpretation of measurements, equilibrium conditions of cells, structure of plasma membrane, and the nature of the process of diffusion are summarized in the first seven chapters. The permeability of membranes to non-electrolytes, weak electrolytes and dyes, gases, water, proteins and large lipid molecules, and ions are dealt with in the next seven chapters. The effects of narcotic substances and temperature are discussed in two chapters. On impedance and potential measurements and permeability, hæmolysis, membrane permeability in relation to secretion, and kidney, there are separate chapters. The last chapter discusses the current theories of cell permeability. There is also an appendix on the theory of penetration of a thin membrane by Dr. Danielli.

We may agree with Newton Harvey who states in the foreword as follows: 'Cell physiology will be grateful indeed for this summing up of a subject which is destined for rapid development under the stimulus of modern methods of exploring molecular dimensions and molecular arrangement. Viewpoints may differ but the facts remain. These are systematically and logically presented in this timely volume'.

RECENT ADVANCES IN ENDOCRINOLOGY.—By A. T. Cameron, M.A., D.Sc. (Edn.), F.R.I.C., F.R.S.C. Fifth Edition. 1945. J. and A. Churchill Limited, London. Pp. vi plus 415, with 73 illustrations including 3 plates. Price, 18s.

NUMEROUS important advances have been made in this important subject, even within the short period of five years since the publication of the last edition of this book in 1940, and excluding the inaccessible work done in enemy countries; for example in the use of radioactive iodine in elucidating thyroid function, the synthesis of substances similar to but more potent than thyroxine, the elucidation of the function of the parathyroid hormone and the steroid hormones, and fuller recognition of endocrine disorders such as Cushing's syndrome, Fröhlich's syndrome, Simmond's disease, and so on. In the present edition the accounts of such advances have been interwoven with those of the advances in the previous decade or so; more attention has been paid to the clinical aspects of endocrinology. With the help of Sq. Leader L. G. Bell, the book had to be almost completely rewritten, as enlargement in volume was not possible under war conditions, but a perusal of the book shows that nothing of outstanding importance on the subject is omitted.

NOTABLE NAMES IN MEDICINE AND SURGERY.—By N. Hamilton Bailey, F.R.C.S. (Eng.), and W. J. Bishop, F.L.A. 1944. H. K. Lewis and Company, Limited, London. Pp. 212, profusely illustrated. Price, 15s. net

In the everyday contact between the medical and allied professions, as pointed out in the preface, proper names are commonly used, for instance, Lugol's solution, Wassermann reaction, Widal test, Fowler's position, Hutchinson's disease, Roentgen rays, Freud's hypothesis. In this pocket-book the authors have given selected biographical notes of eighty such names, covering the period from the time of Hippocrates and Galen to the present time, and the sketches are illustrated with more than 200 figures. The book is attractively printed in bold type on art paper; all the biographical notes form interesting reading. The price (15s.) is rather high, but perhaps inevitable under existing conditions.

A HISTORY OF COMPARATIVE ANATOMY.—By F. J. Cole, D.Sc. (Oxon.), F.R.S. 1944. Macmillan and Company, Limited, London. Pp. viii plus 524, with 200 illustrations. Price, 30s. net

THE nature and purpose of this book is adequately explained in the author's preface. The author had

planned an exhaustive history of zoological discovery and with this object in view had been studying for years, particularly the almost unknown memoirs of those whom he calls 'the little masters of comparative anatomy'. This task had to be abandoned for the time and the author has decided 'to undertake the less formidable task of re-studying the masters themselves, together with the developments to which their works had given rise. The present volume covers such a field up to the beginning of the eighteenth century'. In the preface the author points out how the tradition of special creation was so firmly established in the minds of men that its validity was not questioned for centuries, in spite of the accumulated mass of details pointing in another direction. The author also points out that while the history of medicine has attracted many workers and writers, the history of science is of recent development, owing much to Sarton and Singer.

The book itself consists of eight chapters under the following titles: The contribution of Greece; Zootomy down to the sixteenth century; the development of craftsmanship; Harvey. The encyclopædists; the new comparative anatomy; the Dutch school; Academies and Societies, the Anatomy Lesson; the Anatomical Museum. Not the least valuable parts of the book are the biographical notices and the extensive bibliography. The book is excellently produced and has numerous curious and interesting illustrations. The author has carried out very excellently the task he set himself.

REGIONAL ANALGESIA.—By H. W. L. Molesworth, F.R.C.S. H. K. Lewis and Company, Limited, London. Pp. viii plus 90, with 42 illustrations. Price, 8s. 6d. net

IN this book the author presents the findings based on his personal experience with regional analgesia in his practice as a general surgeon, and hopes that the book may stimulate interest and help in the selection of method or in the acquisition of skill.

The book contains eight chapters bearing the following titles: general principles; methods of regional analgesia; the upper extremity; the lower extremity; the head and neck; the thorax; the abdomen; spinal analgesia. Practical details, including anatomy, are discussed at sufficient length. The illustrations are on the whole good; the author modestly confesses that a few of the less meritorious ones are drawn by himself.

CASUALTY WORK FOR ADVANCED FIRST-AID STUDENTS.—By A. W. Macquarrie, M.B., Ch.B. (Edn.). 1944. E. and S. Livingstone Limited, Edinburgh. Pp. xx plus 231, with 40 illustrations. Price, 4s. 6d. net

THIS pocket-book has been written for the use of A.R.P. and Civil Defence workers and others who have already qualified in first aid. It contains seven chapters entitled examination and diagnosis; wounds; hysteria and shock; hæmorrhage; asphyxia; the unconscious patient; and transport. Many of the methods described are different from those given in first-aid manuals, but the basic principles are the same. The immediate control of hæmorrhage, the immobilization of badly damaged tissues, and the rapidity of delivery to the surgeon's care are stressed.

A HANDBOOK OF OPHTHALMOLOGY.—By Humphrey Neame, F.R.C.S., and F. A. Williamson-Noble, F.R.C.S. Fifth Edition. 1944. J. and A. Churchill Limited, London. Pp. x plus 333, with 12 plates containing 46 coloured illustrations and 189 text-figures. Price, 18s.

THIS book appeared in 1927; second edition in 1935. The third edition was reviewed in this journal in 1939. The present fifth edition shows no major change either in the text matter or in its arrangement, but some 46 new text-figures have been added. Small additions and alterations have been made, particularly in the

chapters on operations, on therapeutics, and in the section on vitamins in the chapter on general diseases. Particular mention may be made of the chapter on eye diseases in the tropics, which has been rewritten by Colonel Harold Williamson with several additions, and which 'is believed to be of considerable use to many who practise ophthalmology in hot climates'. Unfortunately in this chapter some statements are rather misleading, especially the one about leprosy, 'only ten months are now required at Dichpali to render the average patient non-infective and arrest the disease' (p. 289).

THE DENTAL SURGEON'S HANDBOOK: MODERN DENTISTRY IN DAILY PRACTICE.—By Marzell Bronner, D.M.D., and Max Bronner, D.M.D. 1944. John Wright and Sons Limited, Bristol. Pp. viii plus 250, with 42 illustrations. Price, 21s. net

THE literature on dentistry, as in several other subjects, has become overwhelming, and the authors attempt in this book 'to clarify and simplify the scope of information in the light of the most recent knowledge' and to present the problems of chairside dentistry in a readily accessible form. The book is divided into two parts. Part I entitled 'Handbook' contains seven chapters dealing with the diseases of the teeth, mouth and jaw; bacteriology; materia medica; classification of drugs according to their action; calcification and eruption times of teeth; materia technica; and the last being a miscellaneous one. Part II entitled 'orthodontics in general practice' contains five chapters on errors in diagnosis, in treatment, and in the choice of methods of treatment, use of orthodontic apparatus, and hygiene in orthodontal treatment. A very informative book.

ESSENTIALS OF SURGERY FOR DENTAL STUDENTS.—By J. Cosble Ross, M.B., Ch.M., F.R.C.S. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 284, with 196 illustrations. Price, 20s. net

THE author has been the lecturer in clinical surgery to dental students at the University of Liverpool for a number of years, and his aim in this book, which is intended for the dental student about to embark on general hospital practice, is to cover the syllabus in dental surgery of the Royal College of Surgeons and of the universities of the British Empire. Surgical bacteriology and anaesthesia are omitted. The subject-matter of the book is dealt with in twenty chapters describing the diseases of the sense organs, skin, blood vessels, nerves, bones and joints, glands, of the head and neck, including tumours of dental and non-dental origin. Details of carrying out clinical examinations are given in the first chapter, and radium therapy is described in a separate chapter. The illustrations are numerous and good, some of them being in colour.

HANDBOOK OF DIAGNOSIS AND TREATMENT OF VENEREAL DISEASES.—By A. E. W. McLachlan, M.B., Ch.B. (Edin.), D.P.H., F.R.S. (Edin.). Second Edition. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 371, with 159 illustrations, 20 in colour. Price, 15s. net

In our review of the first edition of this book last year we pointed out that penicillin was not mentioned in it, and that with the present rapid development the book may quickly need revision. It is gratifying to see the second edition so soon, in which the value of penicillin has been adequately brought forward. As stated in the previous review, this is an admirable handbook for students and practitioners.

THE VENEREAL DISEASES: A MANUAL FOR PRACTITIONERS AND STUDENTS.—By James Marshall, M.B., B.S., M.R.C.S., L.R.C.P. 1944. Macmillan and Company, Limited, London. Pp. xi plus 348, with 105 illustrations, some in colour. Price, 21s. net

THE advice of the general practitioner will, in the future, be increasingly sought upon this subject, and

the results obtained by individual treatment, especially in gonorrhoea, can be vastly superior to those attainable in ordinary hospital or clinic practice. Major Marshall, who is now the command venereologist of the Eastern Command and London District, has, therefore, written this book with the object of outlining the basis of diagnosis of venereal diseases and the up-to-date methods of treatment which can easily be carried out in private practice.

The book is divided into four parts: gonorrhoea, syphilis, other venereal and allied diseases, and technique. In each part the subject is discussed in several chapters, excepting part IV, which contains only one chapter on practical instructions concerning technique. The 105 illustrations are excellent; most of them are original and some are in colour. One of the very best of the smaller books on this subject.

VENEREAL DISEASES AND MODERN SYPHILOTHERAPY.—By K. D. Lahiri, M.B., B.S. 1945. Himalaya Publications, Patna. Pp. 193, with 9 illustrations. Price, Rs. 2-15

THIS booklet contains much useful information about venereal diseases. It is not clear why yaws is included among venereal diseases.

ACTIVE PSYCHOTHERAPY.—By Alexander Herzberg, M.D., Ph.D. 1945. Research Books Limited (William Heinemann Medical Books Limited), London. Pp. 152. Price, 12s. 6d.

THIS monograph sets forth the details of a method of psychological treatment which the author has found in many ways more advantageous than the purely psychoanalytic treatments, in a series of about 500 cases during a period of 20 years. The introductory chapter deals with a classification of psychogenic disorders, the objectives of psychotherapy in the treatment of psychogenic disorders, the basis of active psychotherapy, and definitions. Then follow thirty-one quite short but very lucid chapters on the causation and maintenance of neuroses and perversions, measures adopted against them, causation and treatment of relapses of these conditions, cases illustrating treatment of masochism, exhibitionism and homosexuality, the comparative advantages of active psychotherapy, and the special technique of the author. The final chapter states the moral attitude of the author towards his patients. Numerous case histories are included in the text.

Many of the author's theoretical views differ from those of the main psychotherapeutic schools, an important one being that 'the distinguishing characteristic of a neurotic or perverse individual, in the great majority of cases, does not lie primarily in the experiences of his childhood, but in the way in which he digests these experiences, and that this is determined to a great extent by a set of inborn character traits of a non-sexual nature'. The dominant feature in the author's technique is the tasks assigned to the patient. The simple and direct style of the author makes his account of this intricate subject an easy and interesting reading.

REBEL WITHOUT A CAUSE: THE HYPNO-ANALYSIS OF A CRIMINAL PSYCHOPATH.—By Robert M. Lindner, Ph.D. 1945. Research Books Limited (William Heinemann Medical Books Limited), London. Pp. xii plus 259. Price, 21s. net

DR. LINDNER was called upon 'to learn about—and do something about—psychopaths and psychopathic personality' in 1939, and in this connection he started his experiments on hypnoanalysis which he carried on for nearly five years.

In the first thirteen pages the author discusses the psychological, physiological, sociological and political aspects of criminal psychopathy, and in the next nine pages, the history and characteristics and technique of hypnoanalysis. The bulk of the book, 222 pages, 'is literally a verbalization of the stream of consciousness associations of a young criminal psychopath under

prison detention' during forty-six hours of hypno-analytic treatment. Memories of the patient dating from six to eight months of age have been recorded. The author's summary and conclusion, selected bibliography, and index fill the remaining pages.

The progress of criminology has been beset with many failures and the subject is still baffling. We may agree with Sheldon and Eleanor Glueck who in the introduction state that 'the psychiatrist and psychologist of any school of thought or therapy, the alert judge of a juvenile or adult criminal court, the thoughtful clergyman, the criminologist of inquiring mind, the penologist who conceives his job in higher terms than as keeper of a zoo for human derelicts, and the educator of vision should find this work instructive and provocative'.

THE DIABETIC ABC: A PRACTICAL BOOK FOR PATIENTS AND NURSES.—By R. D. Lawrence, M.A., M.D., F.R.C.P. Eighth Edition, with war supplement. 1944. H. K. Lewis and Company, Limited, London. Pp. viii plus 70, supplement, 15. Price, 4s. net

THIS little booklet which first appeared in 1929 and which has had numerous editions and reprintings is written by a physician who himself suffers from diabetes, and is written specially for nurses and for patients suffering from diabetes. It has had a very wide circulation and has been found very useful by many patients. In the present edition several sections have been rewritten and brought up to date.

YOUR FOOD.—By M. R. Masani. 1944. Pudma Publications Limited, Bombay. Pp. viii plus 82. Illustrated. Price, Re. 1

THIS booklet is the first of 'Tata studies on current affairs' which are meant to stimulate interest in some of India's vital problems and to educate public opinion. Based on authoritative sources, the book gives to the public much useful information on the medical, health, economic and other aspects of the food problem in this country from the modern point of view. It is well written and illustrated.

ELECTROCARDIOGRAMS: AN ELEMENTARY ATLAS FOR STUDENTS AND PRACTITIONERS.—By H. Wallace Jones, M.D., M.Sc., F.R.C.P., and E. Noble Chamberlain, M.D., M.Sc., F.R.C.P. Second Edition. 1943. John Wright and Sons, Limited, Bristol. Pp. 56, with 53 figures

THESE two authors with wide experience of the subject have designed this booklet of only 56 pages for the use of the medical student so that 'electrocardiography should not loom too largely in his general knowledge of medicine'; a refreshing statement from the pen of specialists. Abnormal rhythms, heart block, coronary thrombosis, preponderance, miscellaneous cardiac disorders are illustrated by representative electrocardiograms with adequate legends. The electrocardiograph is well described and also the formation of the electrocardiogram. An excellent booklet.

PRE-EXCITATION: A CARDIAC ABNORMALITY.—By Richard F. Ohnell. 1944. Henry Kimpton, London. Pp. 167, with 29 figures. Price, 15s. net

THE sub-title of this book is 'patho-physiological, patho-anatomical and clinical studies of an excitatory spread phenomenon bearing upon the problem of the WPW (Wolff, Parkinson and White) electrocardiogram and paroxysmal tachycardia'. In this book, which forms part of a series, the author presents an exhaustive thesis on a particular cardiac abnormality which he says is not infrequently met with in human beings and which he calls 'pre-excitation'. 'Pre-excitation indicates an additional excitatory spread in the ventricles of the heart coupled to auricular excitation'.

There are nineteen chapters. The first two are preliminary and deal with terminology and history. Chapters 3 to 8 deal with experimental, physiological

and pharmacological studies on man, and chapter 11 with animal experiments. Patho-anatomical observations, frequency, diagnosis, differential diagnosis, prognosis, clinical picture, heredity, and pre-excitation and paroxysmal tachycardia are discussed in detail in separate chapters, and are illustrated with suitable electrocardiographic records. Eighty papers dealing with the mechanism of this condition are reviewed in a schematic survey comprising about forty different hypotheses or suggestions. In support of his own explanation of the phenomenon, the author assumes that in some way a retardation of the impulse from the auricle and of its continued progress via the Bundle of His occurs in the a-v node; the author presents a number of facts in support.

A PROVISIONAL CLASSIFICATION OF DISEASES AND INJURIES FOR USE IN COMPILING MORBIDITY STATISTICS. Medical Research Council, Special Report Series No. 248. 1944. His Majesty's Stationery Office, London. Pp. 168. Price, 3s. 6d. net

IN January 1942 the Medical Research Council appointed a committee to devise a system for collecting and recording statistics of patients admitted to hospital, using a standardized classification of diseases and injuries. This was immediately required for the preparation of the Medical History of the War, as the classifications used for the purpose in the war of 1914-18 were not altogether suited to the present conditions, particularly for achieving close comparability between the morbidity statistics of the three fighting services, the Emergency Medical Services and the Ministry of Pensions; and if it proved satisfactory, it might be adopted as the standard for national records of morbidity in the post-war hospital services.

Several such classifications exist such as the International List of Causes of Death (fifth edition, 1938), the Diagnosis Code of the United States Public Health Service, and the elaborate Standard Classified Nomenclature of Disease (Logie). Canada has a morbidity code based on the International List (1929 edition). The London County Councils and the Welfare Council of New York have compiled coded classifications of diseases for hospital use. There are also the Diagnosis Codes of the Royal Navy, Army and R.A.F. Moreover, a draft classification adhering closely to the International List and the Diagnosis Code of the United States Public Health Service was prepared by the Nuffield Provincial Hospitals Trust just prior to 1942.

For various reasons, none of these was considered suitable for general adoption in Great Britain, but the committee considered the draft classification of the Nuffield Provincial Hospitals Trust likely to prove useful and have revised and amplified it into the provisional classification embodied in the report under review. In the following three sections, introduction and coding rules, classification of diseases and injuries, tabular lists arranged in the serial order of the International List of Causes of Death (fifth revision, 1938) are given with the applicable morbidity classification code numbers attached. The report also contains a section on therapeutic classification, in the preparation of which considerable use was made of the Standard Nomenclature of Operations prepared by a Committee of the National Conference on Nomenclature of Disease of the American Medical Association, and a section on classification of occupations, included for convenience of reference.

Correspondence

INFECTIVE HEPATITIS AND CATARRHAL JAUNDICE

SIR,—The article on 'Infective hepatitis' by Major N. D. Banerji in the November 1945 issue of your *Gazette* has raised certain points, and I shall be glad if you will ventilate the following views based on an

experience of 32 fatal cases of infective hepatitis which passed through my hands during 1942-45 :—

1. The term infective hepatitis should not be loosely applied. The diagnosis is not easy and the van den Bergh reaction gives no help at all. When clinically a patient proved to be catarrhal jaundice, the laboratory pronounced a biphasic reaction. Again patients brought in an unconscious state and dying the next day gave a prompt direct reaction.

2. Mortality is much higher than 2 in 258 cases reported.

3. Infective hepatitis is a war disease like sprue syndrome.

4. A period of fever, malaise, and signs of bilirubinæmia prior to sudden onset of cholaemia and hepatic failure occurred. Whereas oliguria and albuminuria were not constant, gastro-intestinal symptoms (nausea and vomiting) and nervous symptoms (delirium, insomnia and restlessness) did occur during the closing phases in all fatal cases. In some cases hæmorrhages were also present.

5. Histopathology of the liver revealed 2 distinguishable types: (a) In one type the liver parenchymal cells had disappeared, leaving only the reticular framework filled with dilated venous sinusoids. Here and there appeared well-marked degeneration of liver cells, with stroma infiltrated with inflammatory cells. (b) The parenchymal cells presented a soapy appearance with eccentrically placed nucleus and inclusion bodies not unlike the Councilman type of bodies. My late colleague Major K. Banerji, the District Pathologist, undertook to handle this side of the picture, and I have no doubt that he will publish his paper in the near future.

6. The treatment laid down for hospitals in Lahore District was repeated administration of a pint of 25 per cent glucose intravenously with insulin 10 units subcutaneously. Once the case commences to slip into the second stage (marked by nausea, vomiting, delirium, insomnia and restlessness) if there is anything which will help it is the above therapy.

7. Sodium salicylate is of distinct help during early phases. I found 10 grains of physiologically pure sodium salicylate in 10 c.cm. of saline intravenously on alternate days, six such, very helpful.

Yours, etc.,

P. V. KARAMCHANDANI, M.B., F.R.C.P.,

LIUTENANT-COLONEL, I.M.S.,

Commanding, C. M. H., Mehgaon.

[Note.—According to Rolleston and McNee ('Diseases of the liver, gall-bladder and bile-ducts', Macmillan and Co., London, third edition, 1929, p. 507): 'Most if not all cases of so-called catarrhal jaundice are due to an infection involving both the bile ducts and the liver cells, that is to say, a combination of hepatitis and cholangitis'. . . . 'Although the majority of cases are mild it must always be remembered that the clinical picture may change and cases of simple catarrhal jaundice suddenly develop all the phenomena of icterus gravis and acute necrosis (yellow atrophy) of the liver'.

Elliott and Nadler ('Practice of medicine' by Tice, W. F. Prior Company, Inc., U.S.A., 1940, p. 102 and p. 104) sum up the situation as follows: 'Ordinary catarrhal jaundice is believed to be frequently due to the degeneration of the liver with multiple areas of necrosis. The most severe types of acute hepatitis show a diffuse acute necrosis (yellow atrophy). . . . 'Classical acute yellow atrophy appears to be simply a fulminating type of a disease that also occurs in a mild form which may produce no symptoms during the acute stage but which ends in cirrhosis. It has been shown that acute, subacute and chronic forms occur with the same underlying pathology.'

Reference may also be made to an article entitled 'Catarrhal jaundice and acute yellow atrophy of the liver' by Greval and Gupta (1945), *Journ. Ind. Med. Assoc.*, Vol. XIV. No. 10, pp. 216-17.—Editor, I.M.G.]

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL M. S. JOSHI is appointed Honorary Surgeon to the King, 6th March, 1945, *vice* Major-General J. S. S. Martin, C.S.I., retired.

The Viceroy and Governor-General has been pleased to make the following appointments on His Excellency's personal staff :—

To be Honorary Surgeons

Colonel E. Cotter, C.I.E., 11th June, 1945, *vice* Major-General W. E. R. Dimond, C.B.E., C.I.E., vacated.

Colonel R. A. Logan, O.B.E., I.M.S., 19th June, 1945, *vice* Major-General D. V. O'Malley, O.B.E., vacated.

Lieutenant-Colonel J. H. Hislop, I.M.S. (retired), is appointed as Officer on Special Duty under the Director-General, Indian Medical Service, for carrying out the survey of Medical facilities available in certain Rajputana States, with effect from the forenoon of the 4th October, 1945.

Lieutenant-Colonel M. P. Atkinson is appointed as Residency Surgeon, Hyderabad, with effect from the afternoon of the 10th November, 1945.

The services of Lieutenant-Colonel L. K. Ledger, O.B.E., an Agency Surgeon, are placed at the disposal of the Government of Central Provinces and Berar, with effect from the forenoon of the 12th November, 1945.

Lieutenant-Colonel L. K. Ledger, O.B.E., Residency Surgeon, Hyderabad (Deccan), has been appointed as Inspector-General of Civil Hospitals, C. P. and Berar. He assumed charge in this province on 12th November, 1945.

Lieutenant-Colonel W. Scott, who was officiating as Inspector-General of Civil Hospitals, C. P. and Berar, has been reverted as Civil Surgeon and Superintendent, Robertson Medical School, Nagpur.

Lieutenant-Colonel A. S. Garewal, on reversion from military duty, was placed on special duty in the office of Inspector-General of Prisons, C. P. and Berar, from 15th November, 1945, to 21st November, 1945, and assumed charge as Inspector-General of Prisons, C. P. and Berar, from 22nd November, 1945.

Lieutenant-Colonel M. K. Afridi, O.B.E., is appointed Officer on Special Duty (Anti-Malaria) in the Office of the Director-General, Indian Medical Service, with effect from the 24th November, 1945.

Major G. E. S. Stewart, Senior Medical Officer, Port Blair, has been appointed as Superintendent, Cellular Jail, Port Blair, in addition to his duties as Senior Medical Officer, with effect from the 8th October, 1945.

Major E. L. Jones, Assistant Director-General, Indian Medical Service (Recruitment), is appointed Additional Deputy Director-General, Indian Medical Service (Special Insurance), with effect from the 1st November, 1945.

Major M. Sendak, O.B.E., is appointed Senior Medical Officer, Andaman and Nicobar Islands, Port Blair, with effect from the date he assumes charge of the post. He is also appointed Superintendent, Cellular Jail, Port Blair, with effect from the same date in addition to his other duties as Senior Medical Officer.

LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

To be Captain

John Boyce Stafford. Dated 13th March, 1945.

The undermentioned officer of the Indian Medical Service (Emergency Commission) is seconded for service with the R.I.

Captain M. E. Winters. Dated 2nd August, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

To be Captain

Abdus Samad. Dated 15th August, 1945.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

To be Captains

(Miss) Evelyne Veronica Tobit. Dated 17th July, 1945.

(Miss) Eunice Halen Adolphus. Dated 23rd August, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

T. Kadirvelu. Dated 18th July, 1945.

M. P. Mathur. Dated 14th August, 1945.

H. C. Mitra. Dated 20th July, 1945.

15th August, 1945

V. K. Bopardikar. S. V. Sunthakar.

M. C. Adhikari.

To be Lieutenants

S. C. Pant. Dated 1st August, 1945.

Pillarisetty Seshagiri Rao Naidu. Dated 12th August, 1945.

14th August, 1945

Kapur Singh Ahluwalia. Gian Singh Ahluwalia.

Kalim Mahmud Murad. Swadesh Bhagat Rajpal.

Khariti Lal Chopra. Ishwar Chandra Khann.

Pawan Kanwar Garg. Bishnu Dutta Tiwari.

15th August, 1945

Santosh Kumar Mazumdar. Dated 16th August, 1945.

Nirendra Chandra Das. Dated 17th August, 1945.

LEAVE

Lieutenant-Colonel W. Scott, Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, is granted leave for 6 months *ex-India*, with effect from 20th December, 1945, afternoon.

PROMOTIONS

The undermentioned officer is granted the local rank of Major-General, without effect on pay and pension whilst employed as Surgeon-General with the Government of Bombay:—

Colonel A. H. Harty, C.I.E. Dated 15th October, 1945.

Majors to be Lieutenant-Colonels

M. L. Ahuja. Dated 11th November, 1945.

T. C. Ramchandani. Dated 12th November, 1945.

Major Jaswant Singh is granted the acting rank of Lieutenant-Colonel while holding the post of Deputy Director, Malaria Institute of India, Delhi.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain to be Major

S. K. Roy. Dated 11th October, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commissions)

Lieutenants to be Captains

M. A. Shakur. Dated 21st November, 1941.

(This is in supersession of all previous notifications on the subject.)

A. K. Ghosh. Dated 2nd September, 1945.

3rd September, 1945

B. V. S. Rao. K. N. R. A. Rao.

B. S. Nagaraj. Q. A. K. M. Khalaque.

A. B. Shome. Dated 5th September, 1945.

A. K. Ganguly. Dated 6th September, 1945.

F. A. Saldhana. Dated 8th September, 1945.

G. C. Dhar. Dated 15th September, 1945.

S. Kundu. Dated 28th September, 1945.

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Miss) E. M. Hugill. Dated 22nd July, 1945.

(Miss) N. Rogers. Dated 15th September, 1945.

(Miss) D. F. MacBean. Dated 15th September, 1945.

(Miss) B. Howarth. Dated 15th September, 1945.

(Miss) Q. V. Norris. Dated 22nd October, 1945.

(Miss) I. B. Schooling. Dated 18th August, 1945.

RETIREMENT

Colonel W. C. Spackman. Dated 11th June, 1945.

RELINQUISHMENTS

INDIAN MEDICAL SERVICE

(Emergency Commission)

Major W. A. B. Reynard relinquishes his commission on account of ill health, 15th June, 1945, and is granted the honorary rank of Major.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

Major C. Shepherd, 25th October, 1945, on grounds of ill health and is granted the honorary rank of Major.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

Captain (Mrs.) M. Lawton, 7th October, 1945, and is granted the honorary rank of Captain.

Captain (Mrs.) G. E. Harland, 22nd October, 1945, and is granted the honorary rank of Captain.

Lieutenant (T/Capt.) L. E. Wharton relinquishes the local rank of Captain on vacating the appointment of Deputy Assistant Director-General, Indian Medical Service, under the late E. H. and L. Department, 3rd April, 1945.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

PENICILLIN THERAPY COMPARED
WITH SULPHONAMIDE THERAPY IN
CEREBROSPINAL FEVER *

By S. G. VENGSARKER, M.D., F.C.P.S.

V. C. MANKODI, M.B., B.S.

and

D. D. VAIDYA, M.B., B.S.

(The City Fever Hospitals, Arthur Road, Bombay)

RECENT medical literature contains numerous reports on the treatment of meningitis with penicillin, with sulphonamides, and with sulphonamides and anti-meningococcal serum. The following are some recent publications on the subject.

Dawson and Hobby (1944) reported on the use of penicillin in 100 cases out of which only 2 were of meningococcal meningitis. In one case the response was satisfactory; in the other penicillin was not given intrathecally and the patient subsequently responded to sulphonamides and anti-meningococcal serum. A preliminary report on 65 cases of meningococcal meningitis with only one fatality is recorded by Rosenberg and Arling (1944). On the other hand, Meads, Harris, Samper and Finland (1944) treated 9 cases of meningococcal meningitis with penicillin administered both intrathecally and intramuscularly and found that the response was slower than with sulphonamides, and that there were certain strains of meningococci which were resistant to penicillin. White, Murphy, Lockwood and Flippin (1945) treated 12 cases of meningococcal meningitis with penicillin in which there were 6 deaths.

Geffer and his colleagues (1943) found a mortality rate of 6.7 per cent in 45 patients treated with sulphamerazine while with sulphadiazine the mortality rate was 12.5 per cent. Lepper, Sweet and Dowling (1943) treated 22 cases with sulphamerazine and the same number of cases with sulphadiazine; the mortality rate in each series was 9.1 per cent. Appelbaum and Nelson (1944) treated 141 cases with sulphadiazine out of which 139 recovered and 2 died (1.4 per cent).

Appelbaum and Nelson (1944) treated their cases with sulphadiazine combined with anti-meningococcal serum, but found no particular benefit by the combined treatment.

One hundred and sixty-nine cases of meningococcal meningitis were admitted for treatment at this hospital from December 1944 to August 1945, and, without any selection, 70 of them were treated with penicillin, 70 with sulphadiazine,

and 29 with sulphadiazine combined with anti-meningococcal serum.

Clinical features.—The patients in our series presented classical signs and symptoms of cerebrospinal fever, viz, acute onset of fever associated with headache, vomiting, neck rigidity, and a positive Kernig's sign. The patients who died within forty-eight hours of admission were excluded from the series for obvious reasons. According to their clinical condition the patients were classified as 'mild' or 'toxic'. In the penicillin series there were 19 mild cases and 51 toxic cases, and in the sulphonamide series 14 and 56 cases respectively.

The condition of the patients on admission, whether unconscious or semi-conscious with or without delirium and restlessness, is shown in the following table :—

	Total cases	Unconscious	Semi-conscious with delirium	Semi-conscious without delirium
Penicillin series ..	70	16	21	33
Sulphadiazine series	70	12	17	41

The duration of the disease prior to admission varied from 12 hours to 6 days, average 2 days. The onset was sudden in 67 cases and gradual in 3 in the penicillin series; in the sulphadiazine series it was sudden in 58 cases and gradual in 12. The temperature on admission varied from 98°F. to 104°F., average 100°F. The cerebrospinal fluid was turbid in 67 and hazy in 3 cases in the penicillin series, and turbid in 61 and hazy in 9 in the sulphadiazine series. It showed the presence of Gram-negative intra- and extra-cellular diplococci in the ratio of 1:4. There was a concomitant increase in the cell count with polymorphonuclear cells predominating (85 to 95 per cent). The proteins were increased and the sugar was either diminished or absent.

There were no complications in the course of the disease in the penicillin series, while there was only one complication, facial nerve paralysis of the lower motor neurone type in the sulphadiazine series for which anti-meningococcal serum was given.

Penicillin therapy.—(a) *Intrathecal injections.* An initial diagnostic lumbar puncture was done on admission, and if the fluid was turbid an intrathecal injection of 10,000 units of penicillin diluted in 10 c.cm. of distilled water was given. This was continued daily till the cerebrospinal fluid was sterile on culture, the cell count came down to about 25 per c.cm., and sugar reappeared. From 2 to 15 intrathecal injections were required in this series of cases. In the majority it was given once a day for 4 days, but in more acute cases it was given twice

* Rearranged and condensed by the editor.

daily. The total dosage of penicillin given intrathecally varied from 20,000 to 115,000 units. We are of the opinion that it should be carried out twice a day as a routine in moderately severe cases in order to shorten the course of the disease; and the total dosage of intramuscular injections required when the drug is administered intrathecally twice a day is found to be much less.

(b) *Intramuscular injections.*—Intramuscular injections were given every three hours in the majority of cases. The initial dose varied between 20,000 and 40,000 units, and was continued with gradually diminishing doses to 10,000 units according to the degree of recovery and the interval between injections was increased from 3 to 4 hours. The decision to stop treatment did not depend upon improvement in clinical symptoms alone but also upon the improvement in the cerebrospinal fluid picture as regards cell count and sugar content besides disappearance of organisms. The total intramuscular dosage of penicillin required varied from 200,000 to 1,770,000 units and the average dose was 760,000 units per case. The cerebrospinal fluid was examined at intervals of 3 to 4 days till it was normal on three consecutive occasions before the patients were discharged.

As suggested in a recent publication, only intrathecal injections were given for the first two days in one case as a trial. As the general condition of the patient did not improve, intramuscular injections were started and the patient recovered; these findings suggest that intramuscular administration of penicillin is essential in the septicæmic stage of the disease.

On the average, 4 days were required for recovery by the combined intrathecal and intramuscular treatment with penicillin, but up to 10 days' treatment was needed in acute cases. Symptomatic treatment was also given to individual cases according to the nature and severity of the symptoms.

Sulphadiazine therapy.—After establishing the diagnosis of meningitis by the initial cerebrospinal fluid examination, sodium sulphadiazine, 50 c.cm. of 25 per cent strength, was given intravenously, and repeated daily in moderately acute cases. Usually the temperature came to normal in such cases within 24 hours and it was not necessary to give a third dose, but sulphadiazine was given orally in sufficient dosage. In toxic and hypertoxic cases associated with delirium it was found necessary to give 2.5 grammes of sodium sulphadiazine intravenously at intervals of every 12 hours for two days till consciousness was regained, or alternatively 5 grammes as an initial dose followed by 2.5 grammes after 24 hours. On an average the total oral dose of 65 grammes was given in 12 days. In some cases as much as 80 to 100 grammes were required. The minimum total dose was 20 grammes and the maximum 104 grammes.

The following precautions were taken during sulphadiazine therapy. Adequate fluid by

mouth, in addition to subcutaneous infusions of glucose saline, was given along with sulphadiazine treatment till toxæmia was relieved. Nicotinamide, 50 mg. per tablet, was given with the sulphadiazine tablets, the number being half the numbers of sulphadiazine tablets. The white cell count was frequently checked for the first four days and later at 3 to 4 days' interval. The urine was carefully watched for the presence of oliguria, hæmaturia, etc. The skin and mucous membranes were inspected for the toxic manifestations of the drug.

Results of penicillin therapy and sulphadiazine therapy compared

Effects on temperature :—

Period within which temperature touched normal	Number of cases in penicillin series	Number of cases in sulphadiazine series
1 day	30	36
2 days	12	18
3 "	8	6
4 "	6	4
5 "	8	3
Between 6 and 9 days.	1	1
No effect	5	2

From the above table it is seen that the response of the fever to sulphadiazine was on the whole better than the response to penicillin.

Changes in cerebrospinal fluid picture.—These are shown in the following table :—

	Average period to reach normal in	
	Penicillin series	Sulphadiazine series
Organisms (extra and intracellular).	3 days	2 days
Proteins	4 "	2 "
Sugar (reappearance) ..	5 "	4 "
Turbidity (disappearance).	4 "	3 "
Cell count	5 "	4 "
Completely normal ..	7 "	5 "

It will be seen that the whole cerebrospinal fluid picture became normal earlier with sulphadiazine therapy than with penicillin therapy.

The other results are compared in the following table:—

	Penicillin 70 cases	Sulphadiazine 70 cases
Number of cases recovered.	63 (90%)	67 (95.8%)
Number of deaths	7 (10%)	3 (4.2%)
Number of resistant cases.	3 (4.2%) (1 died, but 2 recovered when sulphadiazine was substituted).	2 (2.8%) (both died).
Relapses ..	4 (5.7%) (1 died; 1 recovered with sulphadiazine and penicillin, and 1 with sulphadiazine only; 1 died on sulphadiazine).	4 (5.7%) (1 died; 1 recovered, and 2 more recovered with penicillin).
Duration of clinical signs (pyrexia, etc.).	5 days	3 days
Duration of specific treatment.	4 "	12 "
Duration of hospital stay.	14 "	* 16 "
Cost of treatment per patient—Hospital stay at Rs. 4 per day.	Rs. 56	Rs. 64
Cost of drug ..	Rs. 96	Rs. 19
TOTAL ..	Rs. 152	Rs. 83

* This apparent increase of stay in hospital in sulphadiazine treated cases is due to the fact that while penicillin therapy could be discontinued with impunity as soon as the patient's condition returned to normal, sulphadiazine therapy had to be reduced gradually during a short period. In cases where sulphadiazine was discontinued abruptly soon after apparent recovery, particularly in children, a tendency towards relapse or chronicity of the disease was found.

Relapses.—It will be seen that the number of relapses was equal in both the series. The indications for relapse in the cerebrospinal fluid picture were as follows in order of occurrence and frequency: haziness, increase in lymphocytes followed by an increase in polymorphonuclears, and diminution of sugar. It was peculiar that in none of the cases of relapse were organisms detected in smear or in culture.

Toxic effects.—No toxic effects were noticed in the penicillin series, except that in almost all cases intrathecal injections were immediately followed by lightning pains of very short duration experienced in limbs and trunk below the site of injection. In the sulphadiazine series, one case developed a morbilliform rash accompanied by rise of temperature, and another case developed agranulocytosis which responded to

a blood transfusion of 250 c.cm. but not to pentnucleotide, nicotinamide or liver therapy.

Sulphadiazine therapy combined with serum.—Twenty-nine cases were treated simultaneously with anti-meningococcal serum and sulphadiazine; 24 recovered and 5 died (17.2 per cent). Usually 50 c.cm. of anti-meningococcal serum were given daily intramuscularly for 3 days. The serum was administered in toxic cases where the response to sulphadiazine was apparently slower as shown by continued rise of temperature and the general toxic condition of the patient. The combined therapy, however, showed no apparent advantage over treatment with sulphadiazine alone. This result agrees with that reported by Emmanuel Appelbaum and Jack Nelson (1944).

Summary and conclusions

(1) A series of 70 cases of meningococcal meningitis each were treated with penicillin and with sulphadiazine. The mortality among the penicillin series was 10 per cent and in the sulphadiazine series 4.2 per cent.

(2) No general or local toxic reactions of any significance were noticed in patients in the group, whereas in one case in the sulphadiazine group there was marked anaemia and granulocytopenia which responded to blood transfusion after an apparently ineffective course of liver, nicotinic acid and pentnucleotide.

(3) In both the groups there were a few resistant cases, some of which responded to substitution of the drug with that of the opposite group.

(4) The clinical and cerebrospinal fluid response to penicillin was slower than to sulphadiazine but the latter drug had to be continued in gradually diminishing doses after recovery, in order to prevent the cases passing into relapse or into chronic condition, especially in children.

(5) The addition of anti-meningococcal to the sulphadiazine treatment produced no particular benefit.

(6) The cost and the present requirement of frequent parenteral administration of the drug in its present form prohibits the use of penicillin except in hospitals.

(7) Combined treatment with penicillin and sulphadiazine or sulphamerazine of the more acute cases not showing satisfactory response to either of these therapies alone is worth a trial.

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ENTERIC FEVERS IN LAHORE

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and

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A LARGE number of cases of fever including some of obscure type is admitted to the wards of the Mayo Hospital every year. During the last three years, the blood of these cases has been cultured as a routine measure and it has been found that quite a large proportion of them are of the enteric type. The following observations are based on the study of these cases. In this investigation the method of blood culture has been used because this is the most conclusive method of establishing an early diagnosis. In enteric infections, the method is particularly useful and is frequently the only means of differentiating typhoid from paratyphoid fevers.

not found to be necessary and was discarded. Two tubes of ox bile were used at one time, one of which contained 1 per cent glucose. This sugar was added because it is generally agreed that the addition of a fermentable carbohydrate favours the growth of an organism. Five c.c. of blood were added to each tube. We gained the impression that there is some advantage in the use of glucose-bile medium. In positive cases there is always growth in glucose bile after 24 hours; in bile without glucose there is usually growth in 24 hours but sometimes it takes 48 hours. Moreover, in one case no growth appeared in bile medium at all whereas glucose bile showed growth. Blood cultures were incubated for 24 hours and then subcultured on agar slopes and in sugar media, namely, glucose, lactose, mannite and saccharose. These tubes were examined after 24 hours' incubation. The growth on agar, if any, was tested on a glass slide for agglutination with typhoid and paratyphoid antisera. Later, the suspension of the growth was tested for agglutination up to the full titre of the serum. In this series, paratyphoid A strains usually did not produce any appreciable amount of gas in the carbohydrate media. If no growth appeared in 48 hours, primary culture media were incubated for 7 days, subcultures on agar and carbohydrate being made daily. In 3 cases growth was obtained after 72 hours but in no other case was a positive result obtained even after 7 days' incubation. It therefore appears unnecessary to incubate the media for more than 72 hours for the enteric group of organisms.

Some epidemiological observations

Seasonal prevalence.—The disease is endemic in Lahore. Throughout the year cases are admitted into the hospital, but the incidence is highest during the months of May, June, July and August. Its greatest prevalence in summer

TABLE I

Monthly figures for enteric fevers in Mayo Hospital, Lahore

Month:	Years			
	1941	1942	1943	1944
January	5	1	3 (1)
February	3	1	1
March	8	0	3
April	7 (5)	4 (1)	5
May	12 (10)	1	17 (1)
June	5 (1)	9 (1)	11 (1)
July	4 [1] <i>B. enteritidis</i>	1 (1)	3 (2)
August	1 (1)	7	11 (1)
September	4	5 (2)	3
October	0	2	3 (1)
November	2 (1)	4	3 (1)	4 (2)
December	7 (1)	6	1	5 (1)
TOTAL ..	9 (2) = 11	59 (17) = 76	35 (6) = 41	69 (10) = 79

(Note.—Figures in brackets refer to cases of paratyphoid A infection. A case due to *B. enteritidis* has already been reported from the department and is not included in this series.)

Technique of haemoculture

After some experience with various media such as glucose broth, bile salt broth, etc., it was found that the best results are given by ox bile containing 1 per cent glucose. This is distributed in test tubes in 10 c.c. amounts. In the earlier part of the investigation 1 per cent peptone was also added but this was

months may be due to the readiness with which food becomes contaminated by flies which are then numerous, and to the rapid multiplication of bacteria in articles of food. Table I shows the monthly incidence of enteric fever as revealed by positive blood cultures.

Age incidence.—Patients at all ages suffer from enteric infection, as is shown in the following table. In this series, the youngest patient was 2 years old and the oldest 62 years.

TABLE II

Distribution of enteric fevers in different age groups

Under 10 years	11-20	21-30	31-40	41-50	Over 50 years
32	90	69	13	1	2

The maximum number of cases is between 11 to 20 and next from 21 to 30 years. The incidence of enteric infections above 40 is extremely low, there being only 3 cases above 40. These figures are in close agreement with those of Napier *et al.* (1942).

Sex incidence.—In the present series there were 157 males and 50 females but no definite conclusion can be drawn from this as female admissions are far less than those of males; firstly due to limited accommodation in the female wards and secondly to an unwillingness of Indian women to seek admission into hospitals. It is possible that the infection is equally prevalent in both sexes.

Relapses.—There were 8 cases of relapse in this series. Six of these were infections with *Bact. typhosum* and two with *Bact. paratyphosum A*.

Mortality.—It will be seen from table III in which the death rates reported by various observers have been tabulated that the case mortality of enteric fevers varies considerably (2.6 per cent to 25 per cent) in different localities.

TABLE III

Mortality from enteric fevers noted by different observers

Locality	Name of observer	Percentage mortality
Madras ..	Minchin	13.7
Bombay ..	Sulakhe	25.0
Secunderabad (Deccan) ..	Rajoo	20.22
Calcutta ..	Napier <i>et al.</i>	2.6
Lahore ..	Present authors	
	(a) Paratyphoid A	Nil
	(b) Typhoid	26.9
		21.9

It may be pointed out that separate mortality figures in typhoid and paratyphoid infections are often not available. It is, however, well known that paratyphoid fevers are much milder than typhoid. Of 207 culturally positive cases treated, sixteen left hospital at their own risk and they have been excluded from the present analysis. Of the remaining 191 cases 156 were due to *Bact. typhosum* with 42 deaths giving a percentage mortality of 26.9 per cent. The mortality in paratyphoid A infections was nil.

Taking mortality from both types of infections into consideration, percentage mortality was 21.9.

It is generally stated that mortality from typhoid fever in Europeans is very high. Our investigation does not support this statement.* We analysed a series of 156 cases from which *Bact. typhosum* was recovered. The results are shown in table IV.

TABLE IV

Mortality and race

Race	Recovered	Died	Percentage mortality
Europeans ..	14	3	17.17
Indians ..	100	39	28.0

The number of cases among Europeans is undoubtedly too small to be of value from the statistical point of view, but a tentative suggestion may be made on the basis of these figures that mortality amongst Europeans is not higher than in Indians. The vast majority of Europeans living in India are protected by a previous T.A.B. inoculation. The higher mortality in Indians as shown above may be due to two factors. In the first place, most of the Indian patients had never been inoculated with a T.A.B. vaccine. Secondly, only those patients who are very ill seek admission to hospitals; thus accounting for the higher mortality rate than that which may be met with in the general population.* Europeans, on the other hand, seek admission to the hospital as soon as they fall ill, and thus receive the benefit of suitable treatment and good nursing from the beginning of a serious illness.*

Bacteriæmia in enteric fevers

(a) *Frequency of bacteriæmia.*—In enteric infections the proportion of positive blood cultures depends upon the stage of disease at which the specimen has been taken. Cultures made in suitable media during the first week of the disease are usually positive (90 to 100 per cent). After the first week, the typhoid-paratyphoid bacilli gradually disappear from the blood stream, at first slowly, then more rapidly though in rare cases positive results may be obtained as long as the fever lasts.

In table V are set out the results of blood cultures in 207 cases. It will be noticed that the percentage of positive cultures is highest in the first two weeks (35.5 per cent in first week and 36 per cent in second week) and that positive results were obtained in the third and even the fourth week of illness. It is, therefore, suggested that blood culture should always be attempted as long as the fever lasts.

* The opinion on the mortality in Europeans appears to remain unchanged when all statements thus marked are considered.—EDITOR, I.M.G.

The frequency with which positive blood cultures have been obtained in India varies a great deal. Rajoo (1942) isolated the causative organism from the blood in 26 out of 256, i.e.

been definitely diagnosed during the first 3 or 4 days of illness than to wait for the agglutinins to appear in the blood at the end of a week or 10 days and even then get a doubtful diagnosis.

TABLE V

The percentage of positive cultures in different weeks. Total number of positive cultures is 207

1ST WEEK				2ND WEEK				3RD WEEK				4TH WEEK				5TH WEEK			
Total number of cases	Positive	Negative	Percentage positive	Total number of cases	Positive	Negative	Percentage positive	Total number of cases	Positive	Negative	Percentage positive	Total number of cases	Positive	Negative	Percentage positive	Total number of cases	Positive	Negative	Percentage positive
200	71	129	35.5	266	96	170	36.0	112	26	86	23.0	64	14	50	21.9	68	0	68	0.0

11.1 per cent. Minchin (1939), however, obtained 37.6 per cent positives in his series of 444 cases. Similarly, Napier *et al.* (1942) obtained 29 positives by blood cultures in 77 cases, i.e. 37.6 per cent. In this series, blood culture was attempted on all cases of pyrexia of uncertain origin admitted in the Mayo and Albert Victor Hospitals during a period of 3 years, and 207 cases were culturally positive out of 710 cases, i.e. 29 per cent. In Minchin's and Napier's series, blood culture was done in specially selected cases and that explains the higher percentage of positive results obtained by them.

In a selected series of 77 cases of fever suspected to be enteric on clinical and serological evidence, positive results were obtained in 40 giving a percentage of 52 which is fairly satisfactory considering that patients usually seek admission long after the onset of illness.

A negative blood culture at the beginning of a febrile illness is an indication of its non-enteric nature. Not one of the cases yielding a negative culture during the first week was subsequently proved to be suffering from enteric infection by repeated laboratory tests. It is our experience, and possibly that of other laboratory workers, that the average medical practitioner in India places too much reliance on the Widal reaction in the diagnosis of enteric infections. He needs to be reminded that blood culture is the method of choice. It is the most reliable method, and it is successful in the early stages of the disease. Early diagnosis is of great help in the control of the disease, and in the treatment of the patient. In positive cases the relatives and attendants can be protected by T.A.B. inoculation. If the infection is due to *Bact. paratyphosum A*, the patient and his relatives can be assured of a good prognosis. Typhoid fever is a serious condition and is dreaded by most people, and, if the culture is negative, the patient and his relatives are relieved of their anxiety. It is therefore much better to get the blood cultured for enteric infection in all cases of fever which have not

Reference may here be made to one other point. It has been stated that bacteraemia in typhoid fever is of longer duration than in paratyphoid fever. Gay (1918), for example, stated that in enteric fever due to *Bact. typhosum* the causative organism was present in the blood for a longer period than in paratyphoid infections. Ledingham (1921), on the other hand, failed to detect any difference in the duration of bacteraemia in typhoid and paratyphoid A infections. In order to reach a definite conclusion on this point it is necessary to culture the blood in a series of culturally proved cases of typhoid and paratyphoid A infections at different stages of the illness. Such data are not available at present, but the following figures (table VI) showing the period of the disease and successful blood culture may be of some interest.

TABLE VI

Times of positive cultures in typhoid and paratyphoid

	Number of cases diagnosed as	
	Typhoid	Para A
Between 1st and 4th day ..	17	5
Between 5th and 8th day ..	53	14
Between 9th and 12th day ..	49	8
Between 13th and 16th day ..	30	5
Between 17th and 20th day ..	11	1
Between 21st and 24th day ..	7	2
Between 25th and afterwards ..	5	0

Since the incidence of typhoid fever is about five times that of paratyphoid A, the above figures do not show any significant difference in the duration of bacteraemia in the two types of infection.

(b) *Relation of temperature to bacteraemia.*—Herbert and Block (1922) analysed the

results of blood cultures in 7,500 cases and concluded that a positive result is rarely to be expected if the patient's temperature is below 102.2°F. They, however, obtained a positive result in one case with a temperature of only 100°F.

In a series of 90 cases, the temperature charts of which were available, it was found that majority of the positive results were obtained in cases who had a remittent fever of 101° to 103°F. or continued fever above 103°F. but 11 positive results were obtained in fever of 100° to 101°F., and 5 with fever as low as 99° to 100°F.

(1934) series of 112 bacteriologically positive cases 19 (16.9 per cent) were of paratyphoid A infection but in most of the cases (69) the diagnosis was based on the results of the Widal reaction. If only those cases are taken into consideration in which culture (clot) was positive (typhoid 41, paratyphoid A 2), the proportion of paratyphoid A fever comes to 4.6 per cent. One of the most careful studies is that of Napier and his co-workers (1942) who analysed a series of 77 cases, in 38 of which the causative organism was isolated. Of the culturally positive cases, only 5 (13 per cent) were due to paratyphoid A. A recent article

TABLE VII

Positive cultures in relation to type and degree of fever

Organism isolated	Mild remittent, 99°-100°F.	Moderate remittent, 100°-101°F.	High remittent, 101°-103°F.	High continued, 103°F. or above	TOTAL
<i>Bact. typhosum</i> ..	4	8	40	27	79
<i>Bact. paratyphosum A</i> ..	1	3	5	2	11

Relative prevalence of different types of enteric fevers.

The term 'enteric fever' is a clinical one, and from the bacteriological standpoint includes infections with a variety of organisms including *Bacterium typhosum*, *Bact. paratyphosum A*, *B* and *C* and other members of the *Salmonella* group. In vital statistics in India, no distinction is drawn between typhoid and other types of enteric fevers. Medical literature abounds in contradictory statements about the relative frequency of the various enteric infections in India. For example, Lakin (1937) writes: 'In tropical countries paratyphoid fever appears to be more prevalent than typhoid. Paratyphoid A is pre-eminent in India and the Orient'. Manson-Bahr (1940) remarks: '*B. typhosus* is practically world wide in its distribution. Paratyphoid A is the most common form of the infection in the East (India, etc.), paratyphoid B fever in Europe'. Turning to the reports of workers in India in recent years one is impressed with the lack of unanimity regarding the relative incidence of the various types of enteric fevers. Several workers have noted the extreme rarity of paratyphoid infections in India. Minchin (1939), for example, in analysing 444 cases of enteric fevers which were treated at the General Hospital, Madras, during 1936-38, found only 3 cases of paratyphoid A and two of paratyphoid B. Sulakhe (1941) holds a similar view, for, in a series of 75 cases studied by him, all cases except one were due to *Bact. typhosum*. These investigations throw doubt on the statement that paratyphoid A infections are common in India. Other workers in this country have, however, reported a higher percentage of paratyphoid A cases. In Soman's

by Karunakaran and Pillai (1942) further emphasizes this view, for they found 10 cases (13.5 per cent) of paratyphoid A infections in a series of 74 cases in which blood cultures were positive.

The proportion of the various types of enteric infections as met with in the present series is as follows:—

<i>Bact. typhosum</i>	172
<i>Bact. paratyphosum A</i>	35
<i>S. enteritidis</i>	1

It will be seen that the proportion of typhoid to paratyphoid fevers in Lahore is 5:1. In other words, 17 per cent of the enteric fevers are due to *Bact. paratyphosum A*. In all these cases the causative organism was isolated by blood culture. This point is of some importance, because in a number of the previous studies diagnosis was based mainly on the results of the Widal test, the interpretation of which is not free from difficulties. In the first place it is noted that different workers have adopted different standards for positive reactions (Soman 1 in 50, Minchin 1 in 200, Sulakhe 1 in 100, Karunakaran and Pillai 1 in 25 for paratyphoid A, and 1 in 50 for typhoid). As the number of Widal positives depends upon the particular titre accepted as of diagnostic significance, the figures of relative incidence of typhoid and paratyphoid fevers as reported by these workers are not strictly comparable. The second difficulty in the interpretation of the Widal reaction is due to the fact that agglutinins to organisms other than the causative organism usually appear in the blood of patients; for example, the serum of a case of typhoid fever may agglutinate paratyphoid A and paratyphoid B organisms in a fairly high dilution. It may, however, be pointed out that

the titre for the infecting organism is usually higher than that for heterologous organisms. In any evaluation of statistical material dealing with this subject, it is important to bear in mind that paratyphoid infections being comparatively mild, patients do not generally seek admission to hospitals. Therefore, an opinion on the relative incidence of the two diseases based on hospital statistics, which are bound to show lower figures of paratyphoid A infection than the actual infection in the general population, is not absolutely reliable. The present investigation, however, shows that paratyphoid A infection (17 per cent) is somewhat more common here than in other parts of India, since the highest figure so far recorded is 16 per cent (quoted by Napier *et al.*). Our impression is that some if not the majority of the cases of fever of short duration met with in general practice may prove to be paratyphoid, if blood culture is resorted to in the earlier stages.

Infections due to *Bact. paratyphosum B* have been reported from certain parts of India. Minchin, for example, found two cases in a series of 444 cases of enteric fevers studied by him. Karunakaran and Pillai (1942) recorded one case in which both paratyphoid A and paratyphoid B were recovered from blood. Seshadrinathan and Pai (1940) in their paper on 'The Vi-agglutination in enteric fever' refer to three cases in which *Bact. paratyphosum B* was isolated. These are the only three reports of paratyphoid B infection which we have been able to collect from the literature in India. In any case, infections with this organism are extremely rare. In our series of 207 culturally positive cases, not a single case of paratyphoid B infection was found, and it is extremely doubtful if such infections occur in this province.

Wasti (1945) has recently reported nine cases of infections with *Bact. paratyphosum C*, in five of which blood culture was positive, and has referred to some more cases from certain parts of India.

Data on the incidence in India of enteric-like fevers due to members of the *Salmonella* group other than typhoid and paratyphoid organisms are not available. Karunakaran and Pillai have set out tables showing figures of infections caused by organisms belonging to the *Salmonella* group other than *Bact. typhosum* and *Bact. paratyphosum A*, but it is a pity that no attempt was made to determine the exact position of these organisms in the Kaufmann-White schema. A case of enteric type, from whose blood *S. enteritidis* (Gaertner) was recovered, was reported from this laboratory (Goyle and Shaikh, 1943).

Mixed infections due to *Bact. typhosum* and other organisms have been reported by several authors, but as most of them did not isolate the organisms from the blood, the exact nature of the causative organisms is not free from doubt (Butler, 1937). In the present series, there were 4 cases which yielded more than one organism.

Of these, two showed *Bact. typhosum* and *Staphylococcus aureus*. Both these cases had extensive bed sores. As repeated culture of blood gave similar results, contamination from extraneous sources could be excluded. The other two were infections with *Bact. typhosum* and *paratyphosum A*. In one of these *Bact. typhosum* was first isolated on 7th day of illness. The temperature came down to normal on 27th day and again rose to 103°F. after 4 days. Blood was cultured on the 24th day of illness and showed *Bact. paratyphosum A*. In the second case the first blood culture was made on the 3rd day of illness when *Bact. typhosum* was isolated. Another blood culture was made on the 33rd day of illness and it showed *Bact. paratyphosum A*. Relapses in these two cases were certainly due to a second type of infection acquired during convalescence.

Summary

(1) In this paper are recorded the results of blood cultures carried out during a period of over three years in 710 cases. Of these, 208 were positive for one or the other member of the enteric group of organisms.

(2) Epidemiological data are given. Enteric fevers are endemic in Lahore; their highest incidence is in the summer months. No age is exempt but most cases occur in the age period of 11 to 20 years. The incidence is apparently higher in males than females. The mortality rate in typhoid infections is 26.9 per cent and nil in paratyphoid A infections. Contrary to the general belief, the case mortality in Europeans was less than among Indians, and reasons for this are suggested.

(3) The highest number of positive results in blood culture was obtained in the first and second weeks of illness.

(4) The subject of bacteraemia in enteric infections is discussed, and the importance of culture of blood in the early diagnosis of these infections is stressed.

(5) In this series there were 172 cases of typhoid fever, 35 cases (17 per cent) of paratyphoid A fever and one case was due to *S. enteritidis* (Gaertner).

(6) The following conclusions are drawn :—
Typhoid infection is common in India.

Contrary to the statement made in British textbooks that paratyphoid fever is the commonest enteric fever in India, workers in India are all agreed that typhoid is the commonest type of enteric infection here. Paratyphoid a fever is fairly common but not nearly as common as typhoid fever; the difference of opinion as to the relative incidence of these two infections may be explained by the possible variation in the incidence of paratyphoid A infection in different localities, and by the different standards of serological diagnosis adopted by different workers.

Cases of paratyphoid B infection rarely occur in this country.

No case of *Bact. paratyphosum C* infection was met with in this series.

It is suggested that for statistical analysis it is necessary to have data based on the isolation of the causative organisms from blood of patients as the Widal reaction is not always reliable.

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A. COMPARATIVE STUDY OF SAPONIN BROTH AND BILE BROTH AS A BLOOD-CULTURE MEDIUM FOR ISOLATION OF ENTERIC GROUP OF ORGANISMS

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SINCE many pathogenic organisms gain access to the blood stream during the initial and acute stages of bacterial infections, their isolation from the blood constitutes an important diagnostic procedure. Many of these organisms have been found to vary considerably in their nutritional requirements; hence the selection of suitable media for their primary isolation becomes particularly important. Moreover, recent work has confirmed the view that single media alone are unreliable for blood culture, and a wide range of media has been recommended.

For the primary isolation of enteric group of organisms from blood, media such as glucose broth, Hartley's broth or bile broth are chiefly used, and preferably the last. During the typhoid epidemic, blood cultures routinely done in bile media occasionally remained sterile and many of these clinical conditions later were shown to be non-enteric in type such as malignant malaria, influenza, typhus fever, pneumococcal or streptococcal infections. It was, therefore, thought that the isolation of the causative organisms in the last two condi-

tions was likely to have been missed due to the routine use of a single medium such as bile broth, which is inhibitory for the growth of streptococcus or pneumococcus. Many workers have independently claimed that the use of saponin greatly enhanced the value of blood cultures. Elliot (1938) studied blood cultures from sixty-five patients immediately after dental extraction, and from four cases of infective endocarditis demonstrated the value of saponin in the blood-culture medium. Penfold and his colleagues (1940) reported on 160 routine blood cultures, using different media including saponin broth, and obtained 33 positive results. Several species of organisms were isolated, the commonest being *Streptococcus viridans* and *Staphylococcus pyogenes*, from cases of infective endocarditis and acute osteomyelitis. Only once were typhoid organisms isolated; these grew on all the media used. Very diverse results were, however, obtained with the use of different media, the results depending on the infecting organism. Since saponin broth was shown by them to be selective for the isolation of the streptococcus, and comparable to other media in the isolation of *B. typhosus*, it was thought desirable to give a wider trial to this medium and to assess its value in the isolation of typhoid and paratyphoid organisms from blood.

Technique

Bile broth was prepared in the usual manner. Saponin broth was prepared by the addition of sodium citrate to nutrient broth to make a two-per cent solution. White saponin (B.D.H.) was added to make a concentration of 0.1 per cent and the whole was sterilized by steaming on three successive days for half an hour and then made up in 10 c.cm. amounts.

Six to 8 c.cm. of blood were withdrawn from a vein and distributed rapidly at the bed-side in portions of 2 c.cm. each to saponin broth, bile broth, and empty sterile test tube for purposes of Widal test. Both the culture tubes were incubated at 37°C., and sub-cultures were taken at the end of 24 hours and for five days if negative.

Results and discussion

Blood cultures were made from patients with fever suggestive of enteric fever. In a series of fifty-two consecutive blood cultures, only seventeen gave positive results. The following species of organisms were isolated: *B. typhosus* in twelve cases, *B. paratyphosus A* in four cases and *B. coli communis* in one case. Out of seventeen positive blood cultures, bile medium could only grow fifteen, the other two being positive with the use of saponin broth. Saponin broth alone could grow only nine positive cultures out of seventeen.

Many of the positive bile cultures showed growth in 24 hours but the growth of *B. typhosus* appeared to be delayed in saponin broth to

48 hours or more. The clot cultures in ox bile showed parallel results with the bile broth except in two cases where bile broth remained sterile. The clot culture results were not taken for comparison because the amount of blood put for clotting varied from case to case. None of the fifty-two blood cultures was found to be contaminated. No Gram-positive organisms, such as streptococcus or pneumococcus, were isolated in this series in spite of the use of saponin broth.

Summary and conclusion

A series of fifty-two blood cultures was done by inoculation of saponin broth and bile broth from clinically suspected cases of enteric fever. Positive cultures were recovered in seventeen cases only. *B. typhosus*, *B. paratyphosus* A and *B. coli* were the only organisms that were isolated. Nine blood cultures were positive out of seventeen by the use of saponin broth, while fifteen blood cultures were positive with the use of bile broth. Saponin broth, therefore, was found to be actually inferior to the bile media for the isolation of typhoid and paratyphoid organisms although it grew two cultures which failed in bile broth.

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PROTEOLYSED LIVER EXTRACT IN THE TREATMENT OF TROPICAL MACROCYTIC ANÆMIA

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THE discovery of Minot and Murphy (1926) of the curative value of mammalian liver in pernicious anæmia led to investigations into the nature of substance or substances present in the liver which are responsible for its hæmopoietic activity. Cohn and his associates (1928) were pioneers in the preparation of potent extracts from mammalian livers, at first for oral use and later for parenteral use. Following the methods of Cohn *et al.*, Ganslen prepared an extract which was marketed by Bayer and Co. as campolon; this product was found to be efficacious in the treatment of pernicious anæmia as well as in other macrocytic anæmias. Dakin and West (1935) and Dakin, Ungley and West (1936) isolated a glucosamine-free polypeptide from the commercial liver extracts containing fraction G of Cohn *et al.*, which they found to be much more potent than the crude liver extract in the treatment of pernicious anæmia. Anahæmin is the name given to such a product marketed by British

Drug Houses Ltd., London. Liver extracts containing Cohn fraction G, *e.g.* campolon, are known as crude liver extracts, while the more purified extracts, *e.g.* the glucosamine-free polypeptide of Dakin and West, and anahæmin, are known as fine liver extracts. In 1937 Jacobson and Subbarow demonstrated that liver contains one primary and three accessory factors; the association of all these factors is necessary for optimum hæmopoietic activity in pernicious anæmia. Later, Wills, Clutterbuck and Evans (1937), by means of ammonium sulphate fractionation, obtained two fractions from campolon; the soluble fraction was effective in curing the macrocytic anæmia of monkeys, and the insoluble fraction, though ineffective in curing the macrocytic anæmia of monkeys, was effective in pernicious anæmia. Napier and his associates (1938) showed that anahæmin is not effective in cases of tropical macrocytic anæmia in doses in which it is effective in cases of pernicious anæmia; but, given in much bigger doses, its efficacy in the treatment of tropical macrocytic anæmia is equal to that of the potent crude liver-extract preparations.

Wills demonstrated the curative value of marmite in tropical macrocytic anæmia as early as 1931. Later, she and her associates (1937) showed that the curative value of marmite was due not to vitamin B₁, B₂ or B₆ contained in marmite, but to some other factor which was soluble in water and 80 per cent alcohol, and was heat stable. Still later, Wills and Naish (1933) showed that vitamin B₁₂ is not the extrinsic factor of Castle and Strauss which is supposed to be absent or deficient in cases of tropical macrocytic anæmia. From the comparative effect of crude and refined liver extracts in cases of tropical macrocytic anæmia, most workers have concluded that this missing factor is present in much higher concentration in the crude extract. Therefore, the present-day tendency is to use preparations of crude liver extract in the treatment of tropical macrocytic anæmia. Our experience, and the experience of some others, have suggested that adequate protein intake greatly helps the recovery of patients with tropical macrocytic anæmia.

The note by Davis *et al.* (1943) on the efficacy of proteolysed liver extract in the treatment of pernicious anæmia was, therefore, of great interest to workers in the tropics; for proteolysed liver extract contains a considerable amount of protein in an easily assimilable form and vitamins in addition to the full amount of hæmatinic principle, and is therefore an ideal preparation for the treatment of tropical macrocytic anæmia. It may be mentioned here that this conception of Davis and his associates of using proteolysed liver in pernicious anæmia is a modification of the method advocated by Herron and McEllroy (1932) who used autolysed liver for the treatment of pernicious anæmia.

Herron and McEllroy (1933) claimed that autolysis of liver increased the potency of liver to such a degree that the oral dosage requirement of autolysed liver approaches the intramuscular requirement of other liver preparations. This claim was challenged by Castle and Strauss (1935), who asserted that the potency of liver is not increased but on the contrary decreased by autolysis. After this the use of autolysed liver fell into disuse till Davis *et al.* (1943) showed that proteolysed liver, papain digest of whole liver, given orally, was effective in the treatment of pernicious anæmia. In the following year, Davis and Davidson (1944) further reported that proteolysed liver was effective in some refractory

cases of severe anæmia with megaloblastic reaction of the marrow, whereas cases of macrocytic anæmia with 'dimorphic' erythropoiesis showed partial improvement and aplastic anæmias with hypocellular normoblastic marrow did not at all respond to proteolysed liver extract.

The average composition of the different mammalian livers was determined and found to be as follows (table I):—

yield of dry solid matter was approximately 16 per cent of the weight of raw glands. It was analysed for its contents of total nitrogen, mineral matter and iron. The solid matter obtained from sheep liver digest was found to contain 13.302 per cent nitrogen (equivalent to 83.13 per cent protein), 4.8 per cent mineral matter consisting of 0.044 per cent iron; and that from bovine liver digest 12.15 per cent nitrogen (equivalent to 75.93 per cent protein).

The nature and proportions of the nitrogenous constituents were determined by fractional precipitations and by estimation of nitrogen by Kjeldahl, and amino-

TABLE I
Average composition of mammalian livers

	Moisture, per cent	Total protein, per cent	Fat, per cent	Carbohydrate, per cent	Mineral matter, per cent	Iron, mg. per cent
Buffalo ..	69.42	20.08	2.75	6.22	1.53	23.78
Cow ..	72.58	16.85	5.14	4.00	1.50	30.00
Sheep ..	67.10	18.18	8.07	5.53	1.19	29.00
Pig ..	73.60	15.16	5.77	4.22	1.35	40.00

Proteolysed liver extracts were prepared both from the liver of sheep and cows. The different steps in the preparation are as follows:—

(i) *Collection, weighing and mincing.*—Liver from healthy animals is collected from the slaughter-house in the evening immediately after the animal is killed

nitrogen by van Slyke apparatus according to the methods of Schryver and Buston (1930). The results of the analysis are shown in table II.

(vi) *Ripening, filtration and packing.*—The mixture is kept for 2 to 3 weeks in cold chamber so that the more unstable meta-proteins may precipitate out after being denatured. The mixture is then filtered through

TABLE II

Nitrogenous bodies from different liver digest	Meta-protein, per cent	Proteoses, pri- mary and secondary, per cent	Peptone, per cent	Nitrogenous bodies containing amino- nitrogen (van Slyke), per cent	Nitrogenous bodies giving ammonia, per cent
Sheep liver ..	3.68	Traces	50.30	38.55	7.47
Bovine liver ..	Traces	26.49	15.75	49.85	7.91

and is brought to the laboratory in a container kept cool with ice. The extraneous matter, fat and fibrous tissues are removed mechanically as far as possible, the liver is weighed and then minced. It is next treated with about half its volume of distilled water, is thoroughly stirred and kept in the cold chamber overnight after adding 0.5 per cent chloroform as preservative.

(ii) *Digestion with papain.*—Next morning powdered papain is added to the mixture in the proportion of 2 gm. of papain to every pound of minced liver and another volume of distilled water is added, so that the total volume of distilled water in c.cm. is equal to the weight of the minced liver in grammes. The digestion is done in an enamelled vessel at a temperature of 60°C. for 3 hours with occasional stirring. At the end of 3 hours, the temperature is raised to 100°C. and the mixture is allowed to boil vigorously for 5 to 10 minutes.

(iii) *Filtration.*—The hot digested mixture is filtered through gauze and the filtrate is kept in the cold chamber with the addition of 0.5 per cent chloroform as preservative.

(iv) *Concentration under reduced pressure.*—The filtrate is concentrated under reduced pressure at a temperature not exceeding 60°C. to about one-third of its volume. Alcohol (10 per cent) and glycerine (20 per cent) are added as prescribed in the B.P. 1932 for the preservation of Extractum Hepatis Liquidum. Each fluid ounce of the extract represents approximately 50 gm. of raw liver.

(v) *Analysis of the proteolysed extract.*—A part of the fresh concentrate was dried to solid powder. The

Seitz pads and the filtrate is usually found to be sterile. It is of light red-brown colour, of thin consistency with agreeable taste and odour. It is filled in sterilized ampoules, pulled out at both ends, in lots of 15 and 25 c.cm. and sealed. Kept in the cold chamber the extract keeps well for a long time.

Clinical trials

As a hæmatinic, proteolysed liver extract was given to 15 cases of frankly macrocytic anæmia in the Carmichael Hospital for Tropical Diseases. Sheep's liver extract was used in 4 cases, bovine liver in 11. Details of the cases are shown in table III.

Age.—The ages of the patients ranged from 9 to 50.

Nationality, religion, etc.—Out of the 15 cases, 6 were Beharis, 1 Nepali and 8 Bengalis. There was only one Mohammedan in the group, and the rest were Hindus. All the patients were poor, 2 were destitutes, 4 were from the servant class. Three in the group were strict vegetarians, and the rest were used to a mixed diet.

Dosage.—The daily dosage given in this experiment varied between 30 and 90 c.cm. (extract derived from 50 to 150 grammes of liver). At first, extracts derived from 50 grammes of raw liver were given to the adult

TABLE III
Details of 15 cases treated with proteolysed liver extract

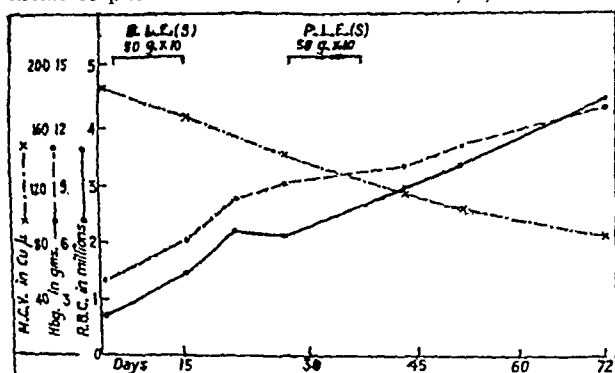
Serial number	Age, race and sex	Spleen, inches	van den Bergh (indirect), mg.	Sternal puncture	Proteolysed liver extract given. Total in gm. of liver	First and subsequent readings of			Interval in days between the two readings	Reticulocyte, per cent. Day of treatment	REMARKS
						Hamoglobin	R.B.C.	M.C.V.			
1	40, M. M.	1	0.8	..	1,300	9.48	2.30	130.4	43	..	Two courses of liver for 16 and 10 days with an interval of 10 days.
2	26, H. F.	6	3.2	Megaloblastic	600	13.75	4.74	84.6	69	5.6	Interval between the two courses was 16 days.
3	40, H. M.	0	0.8	"	1,000	3.71	0.99	136.4	83	11th day 5.9	Fifteen days' interval.
4	22, H. M.	0	0.8	"	Nil	11.00	4.00	84.0	30	..	Patient improved considerably with rest and hospital diet.
						3.98	0.79	183.5	34	..	
5	30, H. M.	0	Negative	..	500	13.06	4.2	97.6	13	..	Slow improvement without further treatment.
						3.57	1.06	160.3	105	18.3	Very good response after two courses within five weeks.
6	21, H. M.	3½	0.8	Megaloblastic	1,390	10.72	3.62	100.7	25	..	Left hospital.
						10.72	3.62	100.7	28	16.3	Poor response even with big dose.
7	30, H. M.	0	Negative	"	1,680	15.10	5.70	80.7	33	..	Good response with big dose.
						10.17	2.89	144.6	42	..	Good response with big dose. Blood transfusion 250 c.cm. on 8th day of treatment.
8	30, H. M.	7	0.4	'Dimorphic'	1,575	11.58	4.00	92.5	56	7.2	Dose increased from 60 c.cm. to 90 c.cm. after 4 days.
						3.16	0.97	134.0	33	..	
9	32, H. M.	2	0.6	Megaloblastic	2,000	15.12	4.8	83.3	42	..	
						9.62	2.34	121.3	56	7.2	
10	24, H. M.	5	2.0	"	2,900	8.52	2.35	106.4	33	..	
						5.22	1.39	136.7	42	..	
11	45, H. M.	7	0.6	'Dimorphic'	5,950	8.93	2.37	113.9	33	..	
						4.40	0.85	158.9	33	..	
12	24, H. M.	0	1.5	Megaloblastic	2,200	13.20	4.62	86.6	26	..	
						3.71	0.76	171.1	35	14.9	
13	9, H. M.	8	2.5	..	1,000	11.41	4.08	88.2	31	..	
						5.50	1.55	141.9	31	..	
14	20, H. M.	Just palpable.	0.4	..	2,900	12.30	3.80	89.4	31	14.9	
						3.43	0.85	135.3	31	7th day 20.5	
15	50, H. M.	2	0.6	Megaloblastic	2,050	10.70	4.49	82.4	31	6th day	
						5.77	1.65	124.2	31	6th day	
						9.35	3.46	92.4	31	6th day	
						2.75	0.67	171.6	31	6th day	
						12.37	4.06	95.5	31	6th day	
						4.4	0.91	153.8	31	6th day	
						11.27	3.49	103.2	31	6th day	

N.B.—The total amount of liver in grammes given to each case is shown in column 6. The amount was given in a single course without any interruption in cases nos. 4, 5, 7, 8, 10, 11, 13, 14 and 15. In case no. 6 it was given in 3 courses and in the remaining cases in 2 courses. The interval between the courses generally varied from 8 to 16 days.

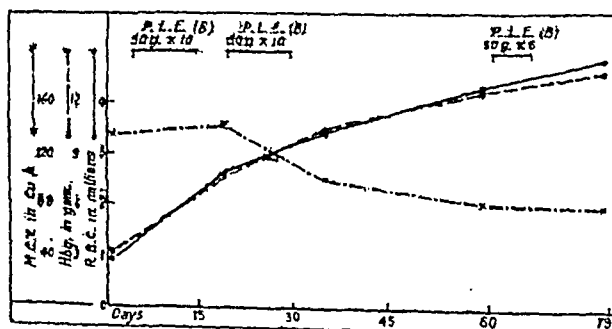
patients in two daily doses for 10 days, and if deemed necessary on subsequent blood examination the dose was repeated for the second and sometimes for the third time. Later, a much bigger dose was given continuously for a long period in a few cases. The total dose used in the experiment varied between 500 and 3,000 grammes of raw liver, except in one case getting nearly 6,000 grammes. The number of days of treatment varied between 10 and 44, but in cases where the extract was given for more than 10 days the treatment was often not continuous. The preparation was well tolerated even in doses of 150 grammes a day, in some cases even in the presence of diarrhoea.

Results.—All the cases showed considerable improvement with proteolysed liver therapy excepting case no. 7 who left hospital against medical advice just after the course and could not be followed up (*vide* table III). Response to treatment of cases nos. 3, 6, 11 and 14 is shown in graphs 1, 2, 3 and 4 respectively.

Graphs showing the effects of oral administration of proteolysed liver extract, on red cell, hæmoglobin and mean corpuscular volume in cases nos. 3, 6, 11 and 14.



Graph 1. Case 3 treated with sheep liver.

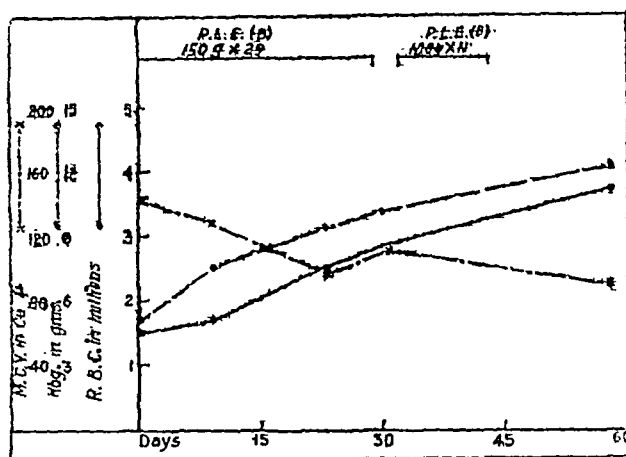


Graph 2. Case 6 treated with bovine liver.

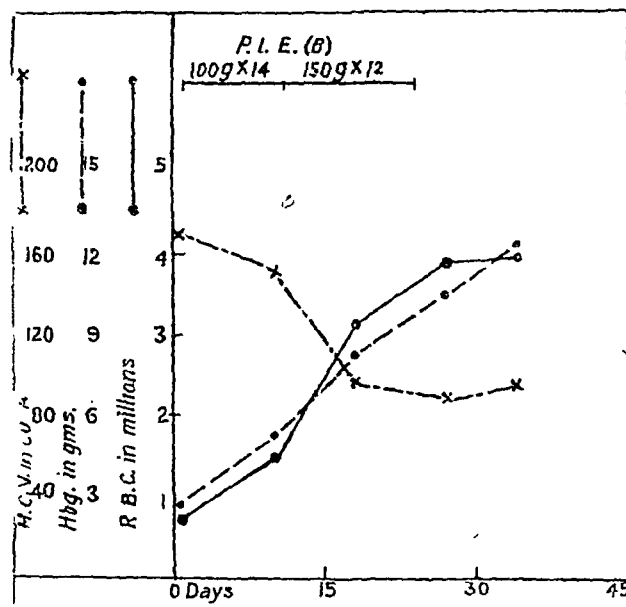
Sundry points

Diet.—We have reasons to believe that the rôle of diet in these cases was only secondary. For, according to our routine procedure, except in very seriously ill patients, proteolysed liver was not given to any patient soon after admission but was only given when there was no appreciable improvement in the blood counts with hospitalization and diet. Moreover, it has been our experience that the improvement with

diet is not seen in all cases, that in the majority of cases the rate and degree of improvement are only slight, that the improvement is appreciably high, as in case no. 4, only in a very few cases, and that all cases of truly macrocytic anæmia require liver in some form or other to bring the blood picture to normal.



Graph 3. Case 11 treated with bovine liver.



Graph 4. Case 14 treated with bovine liver.

Bone marrow.—Sternal puncture was done in 11 cases; in 9 the marrow was megaloblastic in reaction and the remaining two cases showed 'dimorphic' erythropoiesis (Davis and Davidson, 1944), i.e. the condition in the marrow where the majority of the red cell precursors are normoblasts with only a few typical megaloblasts. All the cases with megaloblastic reaction of the marrow reacted very well to proteolysed liver (excepting no. 7 who could not be followed); the two cases with dimorphic erythropoiesis did not react so well with proteolysed liver.

Presence of splenomegaly and hyperbilirubinæmia.—Enlargement of spleen was noticed in 10 out of the 15 cases; the splenic enlargement

was slight in 4 cases, moderate in 2, and huge in 4. The serum bilirubin was generally high in cases with very big spleens but always came down to the normal range with the improvement in the blood picture. Generally, the response to treatment was slower and less in degree in cases with huge spleens.

Gastric acidity.—Gastric analysis was done in 13 cases with the following results: absolute achlorhydria in 2 (nos. 7 and 10), achlorhydria in 1 (no. 12), hypochlorhydria in 4 (nos. 2, 8, 9 and 14), and isochlorhydria in 6 (nos. 1, 3, 4, 6, 11 and 15). There does not appear to be any definite correlation between the state of gastric acidity and the response to treatment with proteolysed liver.

Associated helminthic and protozoal infection.—Helminthic infection was detected in 8 out of the 15 cases, ascaris and ancylostoma in 1 (no. 8), ascaris in one other (no. 9) and ancylostoma in 6 (nos. 2, 4, 6, 12, 13 and 14). Except in one (no. 13), all infections were mild. One case (no. 9) was passing *E. histolytica* cysts while another (no. 3) was passing trophic forms of *E. histolytica*.

No treatment was given for these parasitic infestations and their presence did not seem to interfere in any way with the response to treatment. The one case which did not respond to treatment showed no protozoal or helminthic infection.

None of the patients gave history of malaria; not even those patients with splenomegaly. One patient had an attack of malaria (*P. vivax*) at the end of treatment with proteolysed liver. The attack was promptly treated with quinine, and did not prevent further improvement after the proteolysed liver treatment. Malaria usually produces some anaemia which disappears when the malaria is controlled. In this case it appears that the proteolysed liver therapy even prevented this temporary anaemia during the malarial attack.

Discussion

The above results are very similar to those of Davis and Davidson, viz, that the proteolysed liver is quite effective in small dosage in uncomplicated cases of tropical macrocytic anaemia with megaloblastic reaction of the marrow; complicated cases with 'dimorphic' erythropoiesis are less amenable to treatment and require much bigger dosage and longer period of treatment. These results indicate that the missing factor or factors in tropical macrocytic anaemia is present in proteolysed liver in appreciable amounts. The total dosage required for the effective treatment even of an uncomplicated case would naturally vary, but extracts derived from 100 grammes of raw liver given for 10 to 20 days appear to be sufficient to bring the blood picture to normal in most cases. Oral administration of proteolysed liver is as effective as potent liver extracts given parenterally, thus simplifying the treatment not

only of individual cases but also on a mass scale.

Summary

1. Accounts have been given of the preparation of proteolysed liver and its use in the treatment of tropical macrocytic anaemia.

2. Response to treatment with proteolysed liver in uncomplicated cases of tropical macrocytic anaemia was generally of the same order as that of potent injectable crude liver extracts.

3. Cases with megaloblastic reaction of the marrow generally responded well to proteolysed liver, but cases with 'dimorphic' erythropoiesis did not generally respond to the same extent.

4. Associated mild helminthic infestation and/or infection with *E. histolytica* did not seem to retard the improvement rate appreciably.

Our thanks are due to Dr. S. Ghosh, D.Sc., F.R.I.C., M.B.E., Professor of Chemistry, for providing accommodation in his laboratory and for valuable suggestions for the preparation of proteolysed liver extract.

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ARGEMONE OIL

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ARGEMONE OIL, the oil obtained from the seeds of *Argemone mexicana*, has been used in industrial processes, as an illuminant, and for medicinal purposes. It has an acrid smell and an active therapeutic action. It is found as an adulterant of mustard oil. Its importance as the causative agent of epidemic dropsy has

been studied and reported by several workers (Chopra *et al.*, 1939; Lal *et al.*, 1939). The writer, at the Bengal Public Health Laboratory, has had samples of mustard oil from many characteristic outbreaks of the disease, the outbreaks being confined to groups of persons, *e.g.* the crew of the Calcutta Port Commissioners' launch, 'Gloster', the labourers of a tea garden, the menials employed in a club in Calcutta whose ration of mustard oil was from a stock of oil obtained by the club, and all these tested for argemone oil gave positive reactions.

The presence of argemone oil in mustard oil is due to the adulteration of the mustard seeds. The adulteration is either with argemone seeds only, or it is with mixed seeds in which argemone seeds are present in fair numbers. The argemone plant is ubiquitous in India, growing wild and in poor soils. The seeds are rich in oil, containing as much as 36 per cent of oil (Leukowitsch). As the seeds can be procured in abundance, the temptation to adulterate other costly seeds such as mustard seeds with these exists. The seeds are small, being smaller than most mustard and rape seeds, except the small seeds of *Brassica juncea*. They are black in colour and show a characteristic appearance (Sen, 1941) when examined with a magnifying lens.

The main object of this article is to describe and discuss the special tests for argemone oil.

I. The nitric acid test.—The colour reaction with nitric acid has been long recognized as a test for the pure oil (Leukowitsch), a deep red colour being imparted to the acid layer when equal quantities of the oil and acid are shaken together.

The technique of the test.—Take about 5 mls. of the oil, add an equal quantity of the purest nitric acid free from nitrous fumes; shake so as to mix thoroughly the acid and oil layers; continue shaking for 1 minute; allow the layers to separate. Read the colour of the acid layer as soon as this has occurred. In a positive reaction the acid layer acquires a colour. This is light yellow or yellow when small quantities of argemone oil, such as half to one per cent, are present, and of deeper shades, namely, deep yellow, orange to orange red as the quantity increases.

The nitric acid test is quickly performed and easily read. The three essentials for the test are: (i) a very pure nitric acid, and analytical reagent quality of a reliable maker being recommended, (ii) a quantity of acid equal to that of the oil, and (iii) thorough admixture of the two layers.

The test has fallacies, (a) a yellow colour is also acquired by the acid layer when sesame oil is present, (b) a yellow to orange colour is produced when mustard oil has been coloured by an artificial colouring matter, (c) occasionally a yellow colour is obtained, not attributable to the above causes.

The report (Sarkar, 1942) that many other common adulterants of mustard oil, *e.g.* niger seed oil, safflower oil, cotton seed oil (not kapok oil), also give a colour with nitric acid may be due either to impure or very old samples being used for testing or the nitric acid used being not of proper quality.

Owing to the great importance which the test for argemone oil has acquired, the nitric acid reaction will retain its place as an easily performed, preliminary test for it, especially when many samples of mustard oil are being analysed in a laboratory.

II. The cupric acetate test (Lal *et al.*, 1939).—An acidified solution of cupric acetate is known as the Barfoed's reagent; as it is much less readily reduced than an alkaline copper salt solution, it is used to differentiate the strongly reducing monosaccharides from the disaccharides. In the test for argemone oil, the cupric acetate solution is not acidified, the acid being added to the oil when carrying out the test. The details of this test as developed at the Bengal Public Health Laboratory are given below:—

Reagents for the test.—(i) A 3 per cent solution of cupric acetate, the cupric acetate being dissolved in distilled water by warming on a water bath. The solution is sky blue in colour without any trace of green in it. (ii) Glacial acetic acid.

Technique of the test.—Take 5 mls. of the suspected oil and 5 mls. of a known good oil in two test tubes; add 1 ml. of glacial acetic acid to each, shake thoroughly. The oil completely mixes with the acid. Add 2 mls. of the cupric acetate solution to each tube; shake and mix; place in a boiling water bath; shake frequently while in the water bath so that the layers do not separate out. After 15 minutes remove the tubes from the water bath altogether. Allow the layers to separate. Note the colour of the cupric acetate solution.

The colour of the copper solution is sky blue in the control tube. A greenish discoloration indicates a positive reaction. With fair quantities such as 10 per cent of argemone oil, which is seldom if ever found in adulterated samples, the colour becomes yellowish green. No precipitate due to the reduction of the copper solution is produced by this or by smaller quantities.

The cupric acetate test is a good confirmatory test for the presence of argemone oil. Carried out according to the above-stated instructions, it clearly detects 0.5 per cent of it.

III. The ferric chloride test.—The following technique of the test, as found suitable by the writer, has been adapted from that described by Sarkar (1941):—

Reagents—(i) Concentrated	hydrochloric	
acid (pure).		
(ii) Ferric chloride (fresh)	10 gm.	
Concentrated hydrochloric	10 mls.	
acid.		
Distilled water	90 mls.	

Take 2 mls. of the suspected oil, after filtering it free from any suspended impurities, in a test tube and 2 mls. of a good oil as a control. If the preliminary nitric acid test shows that the argemone oil present is small in quantity (say less than 1 per cent), take 4 mls. of the suspected oil. Add to each 2 mls. of concentrated HCl, shake and mix thoroughly. Warm in a boiling water bath for 4 to 5 minutes*, shake again to mix thoroughly while in the water bath. Take out the tubes and add to each 1 ml. of the ferric chloride reagent.† The reagent passes into the acid layer. Mix the reagent and the acid layer well by rotating the tubes between the palms of the two hands. This last step is very important. The tubes must not be shaken disturbing the separated acid and oil layers in order to mix up the reagent. Place the tubes in the boiling water bath and heat for 10 minutes.

A distinct precipitate appears in the course of heating even when 0.25 per cent of argemone oil is present. There is none in the control tube. The precipitate is in the form of characteristic reddish-brown masses floating in the acid layer; more commonly these gather at the acid and oil interface or rarely settle to the bottom.‡ Under the microscope the appearance is even more characteristic, the masses are found to consist of clumps of light brownish-red acicular or needle-shaped crystals§ (see photomicrograph, plate XI).

Mukherji (1942) writing about the ferric chloride test reported certain modifications. These were: (i) no addition of alcohol, (ii) the separation of the acid layer and its centrifugalization, and (iii) the addition of 4 to 5 drops of the ferric chloride reagent instead of 2 mls.

In the experience of the writer: (i) The addition of alcohol is not essential, in fact alcohol retards the formation of the precipitate making it appear more slowly. (ii) The separation of the acid layer does not make the test more sensitive. The procedure does not simplify the test. (iii) The quantity of the ferric chloride reagent can be reduced.

It should be noted (a) that the technique of the test as described by the writer is simpler than that of Sarkar, (b) that the precipitate appears during the process of the final heating for 10 minutes even when 0.25 per cent of argemone oil is present and it is in the form of characteristic clumps, and (c) that the precipitate which has been described by Sarkar as fibrous is really acicular or needle-shaped and is specific for argemone oil.

*The rationale of Sarkar's 2 minutes at 92-95°C. or 1 minute at 92-95°C. is difficult to understand. A simmering or a lightly boiling water bath is just as good for heating.

†A small quantity of the ferric chloride reagent smaller than 2 mls., as recommended by Sarkar, yields a precipitate.

‡A slight precipitate in the acid layer is better seen with a magnifying lens (4X) than with the naked eye.

§A blackish precipitate which settles to the bottom is obtained with sesame oil. Seen under the microscope this consists of blackish granular masses.

Summary.—Three tests for the detection of argemone oil in mustard oil as adopted at the Bengal Public Health Laboratory, Calcutta, are described, and the reagents and the technique of each test are given.

The writer acknowledges with thanks the help of Mr. P. K. Das, Assistant Analyst, who prepared some of the reagents for carrying out the tests.

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PLASMA CELL MYELOMATOSIS

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PLASMA cell tumours of the bone are not very common. The solitary plasma cell tumours of bone and the extra-medullary plasma cell tumours are even less common. A brief review of the literature and the reports of two cases are given herewith.

Shaw (1923) was probably the first to describe a clear case of solitary plasma cell tumour of bone in a man of 29 with a pathological fracture of the middle of the shaft of the humerus. Rest of the skeleton failed to reveal another lesion radiographically. Tests of Bence-Jones proteose were negative.

Walthard (1924) reported a case of plasma cell tumour of the seventh cervical and first thoracic vertebrae with compression of the spinal cord in a man of 55. Symptoms were present for ten months prior to laminectomy. He died after the operation and at autopsy no other tumours were detected.

Zdansky (1927) described a case of plasma cell tumour in the upper third of the femur in a woman of 68, who soon died after a pathological fracture.

Martin *et al.* (1928) described a plasma cell tumour of the neck of the femur in a woman of 56. Bence-Jones proteosuria was not present.

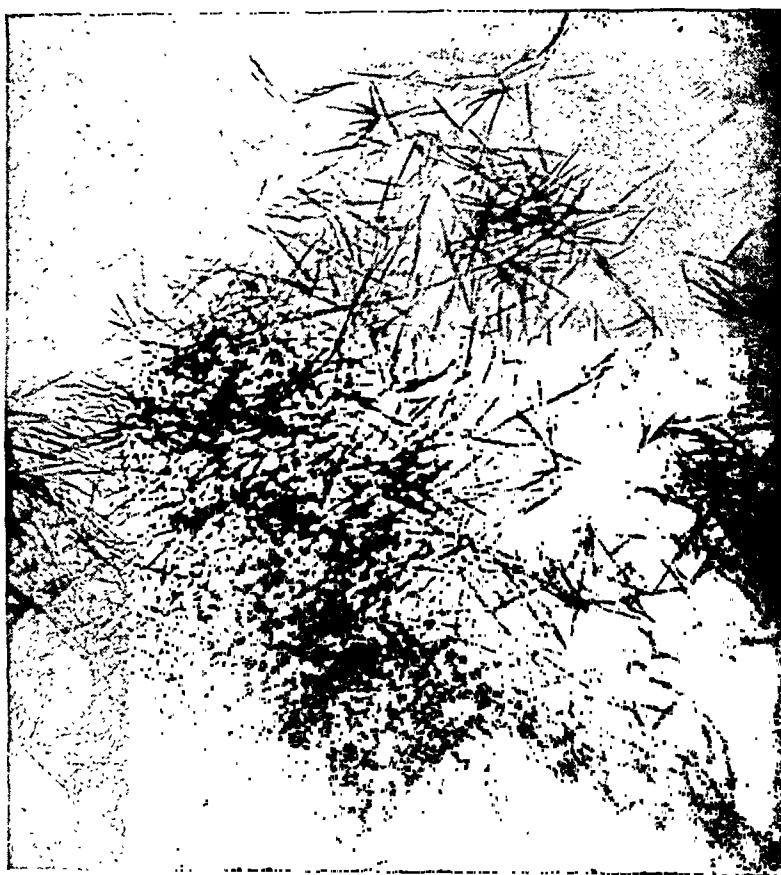
Rogers (1930) reported a case of plasma cell tumour of the shaft of the femur with pathological fracture in a man of 34. Urine was negative for Bence-Jones proteose and radiograms failed to reveal any other bone lesions.

Geschickter (1930) reported a case of plasma cell tumour in the upper third of the femur in which pathological fracture occurred soon after operation. No other such lesions were discovered by radiograms.

Stewart and Taylor (1932) described a proven case of solitary plasmocytoma of the upper third of the humerus with pathological fracture in a man of 34. The case was followed up for eight years and till then he was all right and the repeated x-ray examination showed no other bone to be involved.

Harding and Kimball (1932) reported a solitary plasma cell tumour of the upper third of the femur with a pathological fracture in a man of 60. Bence-Jones proteose was negative in urine, and no other bones

PLATE XI
ARGEMONE OIL : A. K. SEN. PAGE 126.



Photomicrograph of the acicular or needle-shaped crystals ($\times 230$).

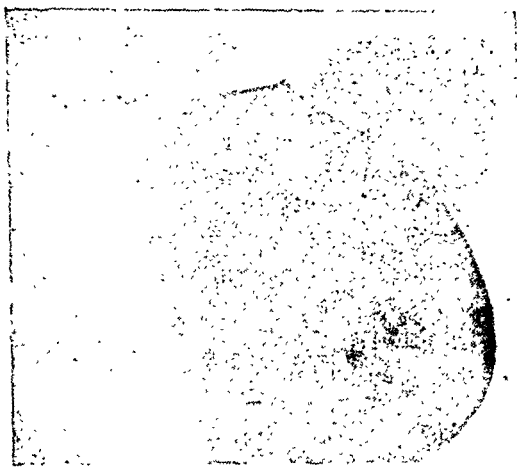


Fig. 1. *Case 2.*—Radiogram of the skull.

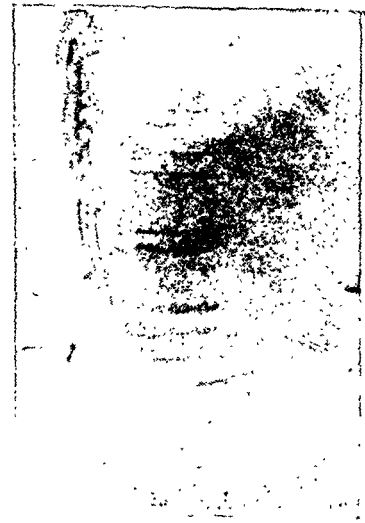


Fig. 2. *Case 2.*—Lateral radiogram of the lower dorsal and upper lumbar spine showing wedging of the 1st lumbar vertebra.

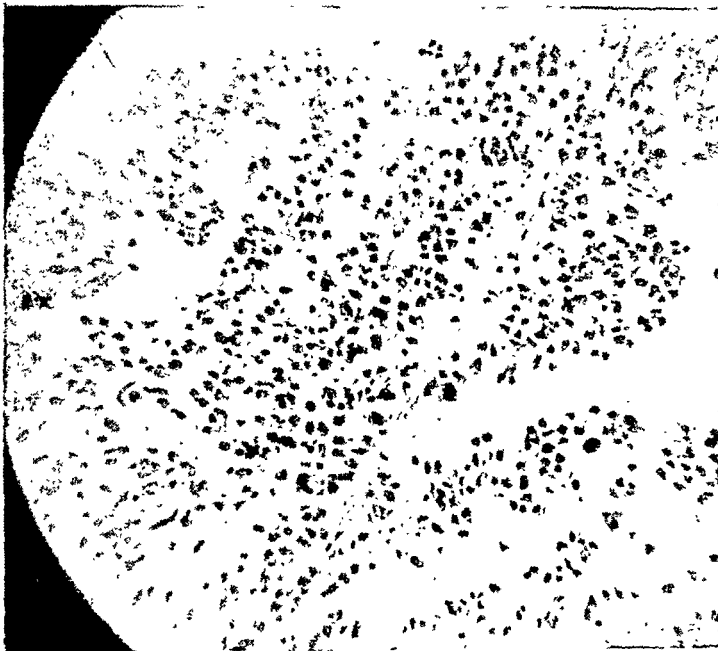


Fig. 3. *Case 2.*—Photomicrograph of paraffin section of tumour tissue stained by hæmatoxylin and eosin. Low power.

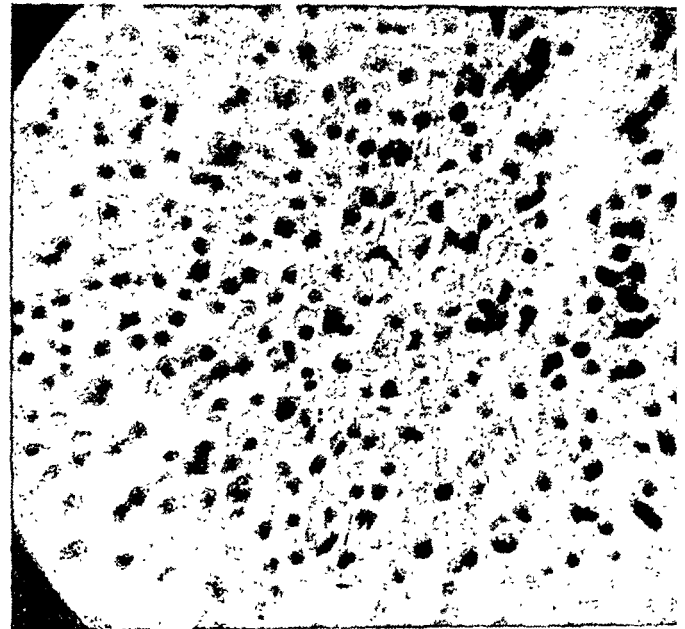


Fig. 4. *Case 2.*—Photomicrograph of the paraffin section showing characteristic plasma cells. High power.

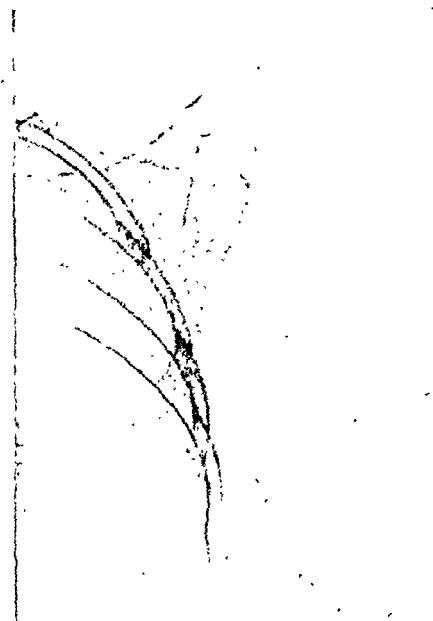


Fig. 5. *Case 2.*—Radiogram of the scapula.

were found to be involved radiographically. Subsequent autopsy confirmed this.

Willis (1941) reported a case of Busser and Lichtenberger (1933) of a woman of 52, with a plasmocytoma of the third lumbar vertebra invading the spinal canal. The patient had this for seven years and then survived for three years after operation, suggesting that the growth was a solitary one. However, no radiograms of the other bones were taken, urine was not tested for proteosuria and no autopsy was performed.

Polson and Shires (1933) described a case of solitary plasmocytoma of the femur in a man of 72, though this was not confirmed by taking radiograms of all the bones and by testing the urine for Bence-Jones proteose.

Willis in his paper on 'Solitary plasmocytoma of bones' reviewed Cutler's two cases of solitary tumours. In one the tumour was in the ileum of a man of 58, general radiograms showed no other tumour and after x-ray therapy the man remained well for 20 months. The second case was one of plasma cell tumour in the second lumbar vertebra of a male negro of 52. Radiograms of the entire skeleton six years after the onset of symptoms failed to disclose any other lesions. He also quotes their third case of solitary tumour of the ileum but doubts it, since, although radiograms of the skeleton are said to have failed to reveal multiple lesions, Bence-Jones proteosuria was present on one occasion.

Leedham-Green *et al.* (1938) reported two cases of plasma cell tumour of the pelvis in men aged 56 and 41, who had symptoms referable to tumour for six years and one year respectively. Radiograms of the rest of the skeleton were negative. Both the patients remained well for 2½ years and 6 months respectively after x-ray treatment.

The same author again quotes a case of Busser and Bugaut (1937) of spinal plasmocytoma in the twelfth dorsal vertebra of a woman of 53.

Willis also quoted a case of Cabot (1938) of spinal plasmocytoma of the seventh and eighth dorsal vertebrae in a man of 70 causing compression symptoms. The solitary nature of the tumour remained questionable due to brief period of observation and because general radiograms were not taken and no test for Bence-Jones proteosuria is reported.

Willis summarized thirteen certain cases of solitary plasmocytoma of bone. They comprised 10 men and 3 women of ages ranging from 29 to 68. The bones involved were femur (5 cases, usually upper third), pelvis (2 cases), vertebrae (3 cases), humerus (2 cases) and tibia (1 case). Involvement of a long bone was associated with pathological fracture in all but one of the cases.

Some interesting cases of extra-medullary plasmocytoma have also been reported.

Newns and Edwards (1944) reported a case of plasma cell myelomatosis with a large renal metastasis and widespread renal tubular obstruction. The patient was a woman of 42 referred for aching chest pain and treated for three years for 'pulled muscle' and fibromyositis. Then she developed small subcutaneous nodules over the interscapular and pectoral muscles and several rounded nodules rather less than 1 cm. were palpable over the scalp. She was unaware of any of these, but for nine months she had observed the development of a similar but larger, firm and painless nodule in the median margin of the left orbit. Besides, the liver and spleen were enlarged and the right kidney was enlarged and mobile and presented a hard smooth swelling in its lower pole. Urine contained a large quantity of albumin, red cell with few hyaline and an occasional granular casts. No special tests for Bence-Jones proteose were applied.

Biopsy of one of the subcutaneous nodules from the chest showed that it consisted of a mass of plasma cells. The patient died, and at autopsy the right kidney was found enlarged and a rounded tumour 4 cm. in diameter was present in the centre of the renal substance. Microscopically the tumour was found to consist of plasma cells. The renal tubules contained casts and foreign body giant cells.

Gordon and Walker (1944) have reported a case of plasmocytoma of the lung in an Italian woman, aged 30, admitted for low-grade temperature following abortion. X-ray of the chest showed a round, sharply circumscribed dense shadow, about 2 inches in diameter located in the upper and inner part of the left pulmonary field. Radiogram of the long bones and the skull showed no abnormalities. Test for Bence-Jones protein was negative. Microscopically, the outstanding feature was the predominance of plasma cells.

Helling reviewed 128 cases of extra-medullary plasma cell tumours. Out of these 110 were from the upper air passage and the conjunctiva. Other sites were lymph nodes, thyroid gland, intestines, kidney, ovary, spermatic cord and the skin.

Report of writers' cases

Case 1.—A Hindu male, aged 55 years, had an injury to the right hip region after which he noticed a swelling in the right buttock which gradually enlarged to about 5 inches by 4 inches. It was soft and fixed. After some time he noticed swelling on his head in the left frontal region, right chest in the 5th intercostal space (3 inches by 1½ inches), and right iliac fossa (3 inches by 2 inches). All the swellings were soft and attached to the bone. The patient on admission complained of pain in the region of the swellings and extreme weakness. The temperature, pulse, and respirations were normal. Blood examination showed leucocyte count of 11,500 per c.mm. with polymorphs 80 per cent, and lymphocytes 20 per cent. Urine examination for Bence-Jones protein was positive. Roentgenographic examination of the skull, and pelvis showed multiple myelomatosis in the skull and pelvic bones. Histological examination of the biopsy tissue showed it to be composed of round or oval cells arranged diffusely with very little intracellular substance. The cell type was plasma cell but pleomorphism was present. A number of cells were large with hypertrophic and hyperchromatic nuclei, while others were typical plasma cells. Some of the cells contained two or three nuclei and were larger. Evidence of mitosis was present. Diagnosis: multiple myelomatosis of the plasma cell type.

Case 2.—A Hindu female, aged 12 years, was admitted to the Thomason Hospital with complaint of a lump on the vertex, developing gradually for 2½ years; and pain in the lower dorsal and upper lumbar spines especially on bending, for one year.

The patient was an apparently healthy young girl with normal temperature, pulse and respiration. The lump on the vertex was 4 inches by 4 inches, soft in consistency and nodular. Skin covering the lump was not fixed but the lump was fixed to the underlying bone. The spines of the lower dorsal and upper lumbar vertebrae were prominent and tender on pressure. Other systems were clinically normal. Blood examination revealed red blood cells 3,100,000 per c.mm., white blood cells 6,800 per c.mm., polymorphs 53 per cent, lymphocytes 42 per cent, large mononuclears 3 per cent, eosinophils 2 per cent, haemoglobin 7.3 grammes, E.S.R. 18 mm. Urine: Bence-Jones proteose was absent on repeated examinations. Albumin was present. Wassermann reaction: negative. Blood calcium: 12.5 mg./100 c.c. Skiagram of the skull: right parietal bone showed changes suggestive of the myeloma (figure 1, plate XII). Skiagram of the spine (lower dorsal and lumbar): bodies of the 10th dorsal, 1st and 2nd lumbar vertebrae showed marked demineralization. Body of the 1st lumbar vertebra was wedged (figure 2, plate XII).

Histological examination of the lump biopsy showed: cells round or oval or polyhedral in shape and of variable size. The cytoplasm was acidophilic and nuclei were eccentric. In some cells the cart-wheel distribution of chromatin was discernible. Stroma was scanty mostly consisting of hyaline acidophile material. Extensive areas of degeneration were present (figures 3 and 4, plate XII). Diagnosis: plasma cell type of myeloma.

During the stay in the hospital she developed another lump on the scapula (figure 5, plate XII).

Comments

Myelomatosis is usually found in adults. Willis in his review mentions the lowest age of recorded cases as 29. Our case 2 was of 12 years, and this we think is the lowest age recorded. In the same case Bence-Jones proteose was absent in the urine on repeated examinations. This is reported to be always present in multiple myelomatosis but absent in solitary plasmocytoma. Willis (1941) laying stress on this finding wrote: 'If proteosuria has been regularly absent for one year from the tentative diagnosis of solitary plasmocytoma, it is improbable that signs of generalized myelomatosis will appear later'. Our second case was admitted to the hospital with symptom of tumour of the vertex only, and Bence-Jones proteose was absent. During her stay in the hospital, she developed another tumour over the scapula and x-ray revealed involvement of vertebræ also. The Bence-Jones proteose was all along absent. The absence of Bence-Jones proteose, though an important point in favour of solitary tumour, should not be entirely relied upon, but radiographic evidence should be the final word against generalization. Urine examination revealed the presence of albumin which could not be due to bone myelomatosis. Is extra skeletal involvement of kidneys present? The question can only be decided at autopsy. This is not possible as the patient is still living and is improving under x-ray therapy. Her vertex mass is reduced by 50 per cent. This good effect of x-ray therapy has also been reported by other authors. The serum calcium in case 2 was high and this increase has also been reported by other authors. The radiographic characters of plasmocytoma are not distinctive. This tumour has been mistaken for endosteal sarcoma and for giant cell tumour. It can also readily simulate the appearances of a metastatic growth. Willis has emphatically pointed out this fact and emphasises the necessity of ultimate diagnosis of plasmocytoma by biopsy examination.

The case 2 brings out this point very well as the radiographic appearance of the scapular tumour is not characteristic of plasmocytoma.

Summary

Two cases of plasma cell myelomatosis with a review of the literature are described. One case has low age incidence and absent Bence-Jones proteose.

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NEEDLE BIOPSY OF THE LIVER

TECHNIQUE AND DIAGNOSTIC APPLICATION

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THE large number of laboratory tests which have been proposed to evaluate the functional status of the liver clearly indicate that no single test is in itself either perfectly reliable or diagnostic.

Cases of liver diseases with or without presence of outspoken clinical signs, such as jaundice or ascites, are commonly present in the wards and despite the innumerable tests done for the patient the physician often finds himself without a diagnosis. Any safe and reasonably sure diagnostic method would therefore be welcome. Aspiration of the liver to obtain material for histologic study, though not a new procedure, came to prominence as the most important single diagnostic method of liver affections, after the publication of a series of 160 aspiration biopsies by Iversen and Roholm (1939). However, this method not being considered without risk to the patient (Dible, McMichael, and Sherlock, 1943) and failing to obtain sometimes an adequate sample of liver (Hoffbauer 1945; Iversen and Roholm, 1939) has not yet come into popular use in the diagnosis of liver enlargements.

Proper selection and preparation of the patients and substitution of the aspiration biopsy by needle biopsy, using the Vim-Silverman needle, have overcome these objections, and I now believe that needle liver biopsy has a definite place in elucidation of baffling liver diseases. This method has often permitted accurate diagnosis in instances when laboratory and clinical findings were inconclusive.

According to Hoffbauer aspiration, liver biopsy was first brought into use, probably by Lucatello who, however, did not fix or stain the tissue obtained and as such it did not prove of much value in diagnosis. Bingel (1923) and Olivet (1926) reported on a series of liver biopsies, with three deaths, two to hæmorrhages and one due to peritonitis. Iversen and Roholm (1939) published their series of 160 liver biopsies and revived the interest in this method of diagnosis.

They use a needle 18 cm. long and 2 mm. wide, and insert it through the ninth intercostal space in the right posterior axillary line into the liver. The obturator is then withdrawn and suction applied by means of a Record syringe. A small plug of tissue is usually drawn up into the needle.

Baron (1939) suggested an anterior approach to the liver below the rib margin in his report on 48 aspiration biopsies. One of the cases died of hæmorrhage. Chiray, Fiessinger and Roux (1941) also used the anterior approach in their 41 cases. They recommended a trocar 6 cm. \times 1.5 mm. and entered the liver to a depth of 2 cm. only. They failed to obtain material in nine cases and recommended that this method be used only in enlarged and easily palpable livers.

Dible, McMichael and Sherlock (1943) reported 126 liver biopsies using a short 2 mm. bore cannula and the intercostal route. Sherlock (1945) reviewed her 264 liver biopsies (including the original 126 reported previously) and gave the technique adopted by her in detail. She suggests the use of a 15 mm. long with 1 mm. bore cannula instead of the original 2 mm. bore. She punctured the liver through the ninth or tenth intercostal space in the anterior or middle axillary line. There were only two deaths due to hæmorrhage in the first series owing to the use of a thicker cannula. Since the adoption of a longer and narrower cannula, no deaths occurred in the second series of 138 cases.

Needle biopsy of the liver using Vim-Silverman needle was also described by Tripoli and Fader in 1941. They used the anterior subcostal route.

Hoffbauer, Evans and Watson (1945) reported 70 cases of needle biopsy of the liver, using subcostal route. In 20 cases they performed needle biopsy with peritoneoscopy. For this purpose they used a longer needle (18 cm.).

Technique of needle biopsy of the liver

The procedure is carried out at the bed-side or in the operation theatre. The latter is preferable as everything is ready for transfusion, if required. As a routine precaution, the bleeding time, clotting time and prothrombin time, and concentration of each patient is determined. In case the concentration of prothrombin is below 70 per cent 5 mg. vitamin K (kapilin) is given intramuscularly. In case it

is 60 per cent 2 such injections are given, and in cases with 50 per cent concentration 2 such injections are given, one each day for three days preceding puncture.

Cases with concentration below 50 per cent are not considered safe. All jaundiced patients are as a routine given vitamin K. In cases of non-obstructive jaundice and in cases where prothrombin concentration is not too low, vitamin K may be given by mouth, e.g. 2 mg. tablets of kapilin three times a day for three days.

A preliminary injection of morphine (dose depending upon the age and condition of the patient) will be found useful to allay apprehension.

Puncture of the liver

In the present series of cases Vim-Silverman needle has been used to do the liver biopsy.

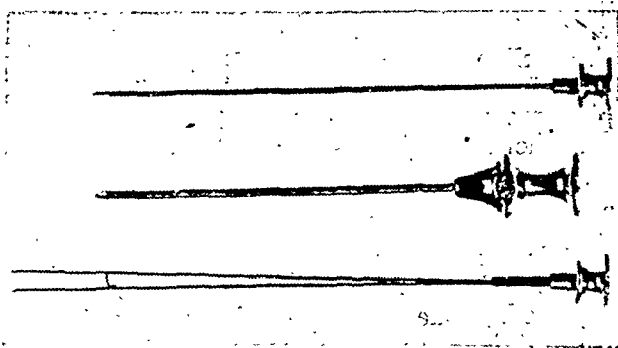


Fig. 7.—Showing the three pieces of the ordinary Vim-Silverman biopsy needle.

In all cases of enlarged and easily palpable liver I have used the anterior route entering the liver below the rib margin. The right upper quadrant of the abdomen is cleansed and the skin is anæsthetized with 2 per cent novocaine or procaine solution. Using a fine-bore needle (3-inch 22-gauge one) infiltration is carried down to the parietal peritoneal surface. Injection of procaine at the peritoneum will render the puncture comparatively painless. The needle is finally advanced to the liver capsule which is then infiltrated. About 10 c.cm. of the local anæsthetic is needed. The liver is entered (as noted by the movement of the needle with respiration) and suction applied to be certain that one is not in an abscess or a markedly vascular area. This needle is then withdrawn. A skin incision 3 mm. in length is made with a scalpel. The Vim-Silverman needle is pushed through the anæsthetized track (the patient having been asked to hold his breath) and inserted about half an inch into the liver substance. The trocar is now withdrawn and the inner-split needle is inserted into the cannula. The inner needle is then pushed its full length so that the two halves of the needle punch out a core of liver tissue. Next the outer needle is advanced, moving over the inner-split needle, thus compressing the two halves and securing

the piece of liver tissue, between the prongs. The outer needle is now rotated once, holding the inner stationary. This helps to cut the tissue core at its base. The two needles are then withdrawn together. The puncture wound in the skin sealed with collodion. The inner-split needle is then withdrawn from the cannula, and between the prongs a piece of liver tissue, varying in length from 1 to 2.5 cm. and about 0.8 mm. in width, will be found. This plug may be fixed in 5 c.cm. of 10 per cent formalin for 12 to 24 hours or in absolute alcohol, if report is not required quickly. If biopsy report is to be given soon, fixation in Bouin's solution is recommended. In cases where liver is not enlarged and easily palpable intercostal route is adopted for puncture. The site chosen is in the ninth or tenth intercostal space in the middle or anterior axillary line. The patient lies supine in bed with the right side as near the edge of the bed as possible. A pillow is placed under the left side tilting the body slightly to the right. The right arm is placed under the head. The skin, pleura, diaphragm, peritoneum and liver capsule are anaesthetized before liver puncture. Rest of the procedure is the same.

After care

This method has been limited to hospital patients and 24 hours strict bed rest is enforced. The pulse is charted hourly for first 24 hours, and the patient is watched for 24 hours after biopsy. If the pulse shows a rise, evidence of hæmorrhage should be looked for. If any sign of hæmorrhage is present, blood transfusion should be given.

The patient may experience mild pain in the right hypochondrium or the right shoulder if the intercostal route has been employed. If necessary a sedative may be given at night. Patient can be up and about after 24 hours, and can leave the hospital after 48 hours.

Difficulties and dangers

There may be failure to obtain a piece of tissue sufficient for histologic examination. Iversen and Roholm (1939) had 10 to 15 per cent failures. Hoffbauer, Evans and Watson (1945) had 30 per cent failure using the Tripoli and Fader (1941) technique. They state that most of their failures occurred in the early stages before the familiarity with the method had been gained. Beck and Haax (1943) state that failure occurred but rarely. Sherlock reported 10 per cent failure in their first series of 126 biopsies and only 2 per cent in the next 138. In my present series there has never been a single failure to obtain liver tissue enough for histologic examination. Another source of difficulty is the presence of ascites where the liver is very ballotable. Paracentesis abdominis should be undertaken in such cases before the liver biopsy is undertaken by the intercostal route. Patient should lie well over on the right

side, thus bringing the liver to the chest wall. In cirrhotic livers, while performing aspiration biopsy, it is possible to extract only a few liver cells leaving the fibrous framework behind (Sherlock, 1945). In needle biopsies, there has never been failure to get the specimen for histologic examination.

The main danger in liver biopsies is hæmorrhage, though it should not be great if the needle is prevented from making liver tear in the parenchyma. Here the intercostal insertion stands at a greater disadvantage than subcostal (Baron, 1939), owing to the fact that a needle inserted between the ribs moving with respiration might cause laceration of the liver capsule and parenchyma. Hoffbauer, Evans and Watson (1945) report that not more than 5 to 10 c.cm. of blood escape before coagulation occurs. They watched the bleeding from the liver as a result of biopsy with Vim-Silverman needle when this was done during laparotomy. The presence of severe bleeding tendency, passive congestion of the liver, suspected liver abscess or suppurative cholangitis is considered a contra-indication to needle biopsy.

Sherlock (1945) has quoted the mortality rates of liver biopsies performed by various authors as follows:—

Author	Date	Number of liver biopsies	Deaths
Ringel	1923	100	2
Olivet	1926	140	3
Huard, May and Joyeux.	1935	163	0
Baron	1939	49	1
Iversen and Roholm	1939	160	0
Tripoli and Fader ..	1941	14	0
Hatieganu, Sparchez, Radu and Macavel.	1943	45	0
van Beck and Haax	1943	200	0
Hoffbauer	1945	65	0
Sherlock	1945	264	2

The combined rate works out to 0.67 per cent. In the present series using the Tripoli and Fader technique there has been one death. This occurred at the beginning in a patient already moribund with cancer of liver. He was absolutely non-co-operative and very apprehensive. Morphine was not given and the novocaine solution used was of doubtful strength. He died of shock and all efforts to revive him failed. Since then the biopsy has been confined to patients who are co-operative. It is essential that patient should not breathe while the trocar is in the liver as a longitudinal rent may thus be produced. Speed in puncture is essential.

Hoffbauer (1945) has used peritoneoscopy in cases with a small or normal sized liver. Rudolck (1939) and Benedict (1944) have described the advantage of peritoneoscopy for the diagnosis and study of disorders of liver. The

Ruddock peritoneoscope is equipped with forceps attachment for biopsy.

Illustrative cases

The following cases will illustrate the diagnostic application of this method in liver diseases.

Case 1.—A Hindu male, aged 45 years, had distension of abdomen off and on for 4 years. On admission his complaints were distension of abdomen, oedema of legs, dyspnoea and cough with expectorations. He was markedly anæmic. There was no jaundice and liver was not palpable. Spleen was palpable 5 fingers below the costal margin. There was ascites, but no other evidence of portal obstruction was present. Laboratory tests showed marked normocytic hypochromic anæmia and raised blood urea. Plasma bilirubin, differential plasma proteins and intravenous hippuric test were all normal. The clinical diagnosis was endemic ascites.

As the trocar and cannula were introduced into the liver for biopsy, the organ felt hard. The histological examination showed disorganization of the liver pattern. The parenchymatous cells showed degenerative changes with deposits of bile pigment in the cytoplasm of cells. There were scattered foci of necrosis and lymphocytic infiltration. This histological appearance suggested subacute hepatitis (see figure 1, plate XIII). This diagnosis was confirmed on post mortem. Liver was small in size (2 pounds in weight) and the surface was granular. It was hard to cut. In this case liver biopsy gave a definite diagnosis, the laboratory tests being equivocal. It also helps to point out that many of the so-called cases of endemic ascites may be really cases of cirrhosis of the liver.

Case 2.—A Hindu female, aged 38 years, was admitted to the Thomason Hospital in March with complaints of fever for 7 months, pain in the abdomen and indigestion for 1 year and attacks of dysentery off and on for 1½ years. She was a poorly nourished woman and markedly anæmic. She had temperature of 99°F. on admission. There was no history of jaundice. Liver edge was felt 6 inches below the costal margin and was firm, smooth and slightly tender.

The spleen was not palpable. There was no ascites or evidence of portal obstruction. Laboratory findings were: plasma bilirubin 0.3 mg. per 100 ml.; blood urea 36.4 mg.; N.P.N. 33 mg.; total proteins 5.24 gm.; differential plasma proteins normal; prothrombin concentration was 100 per cent. The urine contained an excess of urobilin and hippuric acid synthesis was low. Faeces contained urobilinogen. Blood examination showed microcytic anæmia. Except for low hippuric acid synthesis, most of the tests were normal. As the liver was slightly tender and the enlargement started after an attack of dysentery, a working diagnosis of hepatitis (amœbic) was made. Patient was given 10 injections of emetine 1 gr. each with no improvement. Liver biopsy was done and the histological examination showed distortion of liver pattern, degenerative changes in liver cells, and marked increase of connective tissue (see figure 2, plate XIII).

Diagnosis: Portal cirrhosis of the liver.

Case 3.—A Hindu male, aged 50 years, complained of fever for 8 months, epigastric pain, anorexia, cough with expectoration, pain in chest and back. He noticed gradual enlargement of liver since last 6 months and for few days his conjunctivæ had icteric tinge. Liver was enlarged 3 inches below the costal margin. It was hard and tender; the surface was irregular. Spleen was not enlarged. There was no ascites but the epigastric veins were slightly prominent.

Laboratory investigations showed prothrombin concentration of 53.3 per cent and its rise to 66.6 per cent after 20 mg. of vitamin K; W.R. negative; serum bilirubin was increased, urobilin was present in urine and hippuric acid synthesis was 0.4 mg. Liver biopsy showed acini and sheets of cells separated by dense strands of connective tissue. The tumour cells were either cuboidal or columnar and the cytoplasm was oxyphilic. The nuclei were round or ovoid, vesicular,

and showed variations in size. Each nucleus contained a prominent basophilic nucleolus.

Diagnosis: Adenocarcinoma (see figure 3, plate XIII). The liver biopsy confirmed the clinical diagnosis.

Case 4.—A Hindu female, aged 20 years, was admitted to the hospital with fever, pain in epigastrium and right hypochondrium and gradual loss of weight. She had an attack of loose motions with mucus 2 months before admission. She was very weak and slightly anæmic. Liver was enlarged 3 inches and was tender. Spleen was slightly palpable. There was no ascites. Laboratory investigation showed: W.B.C. 7,200 per cu. mm. P—88, L—11, M—1; van den Bergh was biplasmic positive. Urine showed traces of albumin. No abnormal findings were detected in stool examination.

Working diagnosis of amœbic hepatitis was made and 6 injections of emetine 1 gr. each were given. Pain in the right hypochondrium increased and deep icterus developed.

Liver biopsy was done and histological examination showed increase in fibrous tissue with small round cell infiltration. The distribution of fibrous tissue was more unilobular. The bile ducts were dilated and inspissated bile could be seen inside them. This suggested the diagnosis of biliary cirrhosis (infective) (see figure 4, plate XIII) and explained the clinical condition of the patient also.

Case 5.—A Mohammedan female, aged 35 years, complained of painful swelling of right hypochondrium for 9 months, and constipation for last 15 days. She could not retain anything. She was extremely emaciated. There was no jaundice, no ascites and other signs of portal obstruction were absent. There was a swelling in right hypochondrium, reaching up to 7 inches below the costal margin and 3 inches beyond the middle line. It was very hard, irregular and tender. It slightly moved with respiration.

Laboratory investigations showed prothrombin concentration of 61 per cent and its rise to 70 per cent after 10 mg. vitamin K intravenously, blood urea 54 mg., N.P.N. 43 mg.; total proteins 5.75 gm.; serum albumin 3.0 gm.; serum globulin 2.75 gm.; van den Bergh negative; serum bilirubin normal, icterus index 8.5; blood cholesterol 285.7 mg. per 100 c.cm.; total W.B.C. 18,000 per c.mm. P—92, L—8; W.R. negative; urine showed urobilin absent and hippuric acid synthesis was 0.17 gm. Pus cells and albumin was present in urine. Radiography showed no evidence of growth in alimentary tracts and metastasis in lungs. Clinical diagnosis of cancer of the liver was made (see figure 5, plate XIII). The possibility of this tumour arising from kidney was also considered as the mass was most prominent in the right lumbar region and the urine contained albumin and pus cells.

Needle biopsy was done and the histological examination revealed cords of polygonal cells which were cancer cells. It was not possible to say if it was a primary cancer of liver or kidney. Patient died and on post mortem a big rounded tumour (5 inches × 5 inches) was found in the right lobe of liver. On section it was yellowish in colour and degenerative changes were present. Histological examination showed a primary cancer of the liver (adenocarcinoma).

This case illustrates that sometimes biopsy examination may not be able to reveal the source of the new growth if the needle only passes through the growth.

Case 6.—A Hindu female, aged 60 years, was admitted complaining of a painful lump in the right hypochondrium for about 1½ months, loss of weight and marked emaciation. Jaundice was present. There was no ascites or any other evidence of portal obstruction. Liver was enlarged 3 inches below the costal margin. It was tender, smooth and moderately hard. Spleen was enlarged 2 inches, hard but not tender. Laboratory investigations revealed: van den Bergh immediate direct positive; icterus index 35; blood urea 133 mg. per 100 c.cm.; total proteins 0.05 gm. N.P.N. 93 mg.; serum albumin 2.45 gm.; serum globulin 2.6 gm.; prothrombin concentration 80 per cent rising

to 88 per cent after 5 mg. of vitamin K; blood cholesterol 333 mg. per 100 c.cm. Total white cell count was 8,400 per c.mm. P—79, L—19, M—2. Urine examination showed the presence of urobilin in less than 1 in 10 dilution; hippuric acid synthesis 0.25 gm.; faeces of pale colour and urobilinogen was absent.

Radiogram after barium enema showed no abnormality in the large bowel.

Clinical diagnosis of carcinoma of the liver was made. Liver biopsy was done and histological examination showed no evidence of a tumour. The bile canaliculi were dilated and many bile thrombi were present. Liver cells showed cloudy swelling. There were no increase of portal connective tissue. Diagnosis of extra hepatic biliary obstruction was made (see figure 6, plate XIII). In an analysis of this case, one may find clinical and laboratory evidence to support the diagnosis of cancer of liver with jaundice, or cirrhosis of the liver with jaundice or extra hepatic biliary obstruction due to cancer. Consequently, the information obtained by needle biopsy of the liver was of greatest aid.

Other cases

Liver biopsy was performed in a number of other cases. A number of them were suspected on clinical and laboratory grounds to have liver lesion, but showed normal liver histology, especially some cases of ascitis. A case of pulmonary tuberculosis had enlarged liver diagnosed as cirrhotic, but on biopsy showed amyloidosis. One case suspected of kala-azar turned out to be cirrhosis of liver.

Summary and conclusions

The technique of needle biopsy of the liver by Vim-Silverman needle is described. Difficulties and dangers are discussed. Illustrative cases have been described and microphotographs given to demonstrate the diagnostic use of the method.

I am indebted to Major-General H. C. Buckley, I.M.S., Superintendent, Thomason Hospital, Agra, for permitting and giving me facilities for this work in the hospital, to Dr. G. N. Vyas, Professor of Medicine, Dr. K. N. Gaur, Reader in Medicine, Drs. B. K. Dube and K. S. Mathur, Lecturers in Medicine, and Drs. S. Mitra and Ram Pal Singh, for the cases studied, and especially to Dr. Kashi Nath for the constant help.

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A PRELIMINARY STUDY OF SIX-HOUR RAT TEST FOR THE DIAGNOSIS OF PREGNANCY

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THE study herein reported was undertaken to determine the reliability of a six-hour rat test for the diagnosis of pregnancy.

Ever since in 1929 Zondek reported the immature female white rat to be much more sensitive to prolan (the anterior pituitary-like hormone), than the immature female mouse, the rat has been tried as an experimental animal for pregnancy-hormone tests. Eberson and Silverberg (1931), who used immature rats, obtained results as early as thirty-six to forty-eight hours. Walker and Walker (1938) modified the above test and reduced the time to thirty hours. Later, Kelso (1940), and Frank and Berman (1941) published reports on a twenty-four-hour modification, using rats for the diagnosis of pregnancy. The author (1944) confirmed the reports of the above workers on their twenty-four-hour modification, and strongly advocated the use of an immature female white rat as an addition to other test animals, such as the rabbit and the mouse. The twenty-four-hour test period was reduced further to six hours on the basis of which Salmon and his co-workers (1942) established a six-hour rat test for the diagnosis of pregnancy. Ramsey and his associates (1944), and Kline (1944), who reported favourably on the six-hour rat test, found it to be quite reliable and much simpler in performance than the rabbit test. All the authors mentioned above reported between ninety-seven and one hundred per cent accurate results in their observations. The only other equally rapid and reliable test is the one reported from South Africa by Bellerby (1934), and Shapiro and Zwarenstein (1934), who recommended the use of a mature female frog (*Xenopus laevis*) for the diagnosis of pregnancy, the positive reaction being marked by ovulation with extrusion of eggs visible to the naked eye at the end of six hours. The difficulties of importing the special type of *Xenopus* frog precludes any possibility of utilizing it as a test animal in this country at present.

The six-hour rat test has for its basis the production of specific changes in the gonads of the immature rodent as a response to the injection of increased quantities of anterior pituitary-like sex hormone which is present in the urine of pregnant women. The hormone appears in the maternal and foetal circulation shortly after fecundation, and being usually present in sufficient concentration, it gave a positive result within five days of the first missed period of menstruation. The concentration gradually fell during the latter half of pregnancy to become negative about three to

five days after delivery. Evans, Kohls and Wonder (1937) made quantitative determinations of this hormone excreted throughout pregnancy, and reported 150 rat units per twenty-four hours on the third day after the missed period, 6,500 rat units on the tenth day, and a peak of 130,000 or more rat units at about one month, with a rapid decline by the end of the second month to 10,000 rat units or less, and a continuation at this level to the end of pregnancy.

Schoeneck (1936) showed that the smallest amount of urine that gave a positive reaction in normal pregnancy was 0.05 c.cm. The optimum amount varied between 3 and 5 c.cm. Experimental studies carried out at this Institute on white immature female rats by injecting each of them with 4 c.cm. of urine from known positive and negative Friedman samples, showed that it was possible to detect definite hyperæmia, without any appreciable enlargement, of both the ovaries produced by pregnancy urine as early as two hours after the injection, but showing only a 75 per cent accuracy. In four hours, the ovaries appeared definitely enlarged, with marked hyperæmia resulting in a deep red colour. This change was further intensified in six hours, giving a 100 per cent accurate diagnosis. Similar studies with chemically treated and concentrated extracts of urine failed to bring out any advantage over the untreated urine. The results thus obtained and those that were similarly reported by others in the field, stimulated the author to undertake a comparative study of the six-hour rat test and the Friedman test on samples of urine received by the Institute for the diagnosis of pregnancy. Most of the urine samples were received from private medical practitioners, and it was difficult to get a clinical follow-up in every case. Therefore, the Friedman test, known for its accuracy of 98 per cent, was taken as the sole basis for comparison.

The procedure adopted in the performance of the six-hour rat test included all those technical details stressed in a previous communication by the author (1944) regarding the method of collection of urine, the selection of test animals as regards their age and weight, and the criteria applied for reading a positive and a negative reaction. Only one animal was used for each sample, and four c.cm. of urine was inoculated subcutaneously on the dorsum anteriorly and posteriorly. The rat was autopsied at the end of six hours, and the ovaries were examined for a positive or negative reaction. A positive reaction was characterized by enlargement of both the ovaries and marked hyperæmia. With negative reactions, the ovaries remained small, and appeared as only cream-coloured or slightly pink. Occasionally, indefinite or borderline reactions were met with, which would necessitate the use of a second animal. The results of the six-hour rat tests and the Friedman tests were found to be in

complete accord in 96 out of 100 cases. In only 4 cases were the results either indefinite or at complete variance, as shown below:—

Table showing divergent results as obtained by the six-hour rat tests and the Friedman tests

Serial number	6-hour rat test	Friedman test
1	Indefinite Indefinite }	—
2	Indefinite	— —
3	Indefinite	+
4	..	—

It would be quite instructive to find out the reasons underlying the discrepancies shown above. In the first case, the results of both the tests were communicated to the attending physician who reported that his patient was ill with heart and kidney trouble and was delivered spontaneously of a macerated foetus of about twenty weeks' duration. The sample of urine from this case contained 0.18 per cent of albumin, and two rats were used instead of one. In the second case, even before the completion of the rabbit test and on the basis of indefinite result as obtained from the rat test, a fresh sample of urine was asked for, which gave a positive result by both the tests. Obviously, the first rabbit was refractory, and it was proved to be so by injecting a known positive sample. In the third case, not only did the six-hour rat test result prove to be indefinite, but two more rats which were utilized for twenty-four-hour rat tests also gave inconclusive results. The Friedman test, however, gave a definitely positive result. The clinical history of this case was not available. In the fourth case, although both the tests were negative, the attending physician reported, six weeks later, that he found pregnancy on the operation table. It was difficult to comprehend such an occurrence unless it would mean that by unfortunate coincidence both the test animals proved refractory, or the collection of urine sample was faulty. A second sample of urine was requested, but in its absence further investigation remained incomplete.

As pointed out above, in three out of four cases, the six-hour rat test failed to give clear-cut results, the reactions being borderline and difficult of interpretation. In a previous communication on the twenty-four-hour rat test, some of the contributory factors leading to indefinite reactions were mentioned, such as the use of the undersized and unhealthy test animals, the use of urine samples with very low specific gravity or showing the presence of albumin, or abnormal maternal or foetal conditions. The measures to counteract these were

also discussed. In spite of these precautions, occasionally borderline reactions were encountered in the form of slight hyperæmia without any obvious enlargement of both the ovaries. But by keeping to the rule as to what constitutes a positive or a negative reaction, seldom was a diagnosis made contrary to the control test in rabbits. Moreover, a check on the clinical history in such cases usually revealed some abnormal foetal or maternal condition. Any discrepancy between the test result and the clinical diagnosis would be a certain indication to use additional test animals, or to obtain a second sample and repeat the test. Indefinite reactions could also be avoided by extracting the urine samples with ether. Therefore, the occurrence of an occasional borderline reaction need not detract from the value of the rat as a reliable test animal. Kline (1944) reported on 432 tests on 1,011 immature rats, and in only 14 rats (3.2 per cent) did indefinite reactions occur. He also found 2.7 per cent of 482 rats to be refractory. In the present series of 100 tests, done on 120 rats, only one rat was found to be refractory, giving a false negative reaction, while four of them gave indefinite reactions. None of the rats gave any false positive reactions. Two samples of urine were found to be toxic during the test period to rabbits, but the toxicity was not evident on rats which were used for six-hour test. The rats used for 24-hour test, however, died.

The six-hour rat tests showed a perfect correlation with the Friedman tests, and the results just described and analysed confirm the opinion that the rat is not only a suitable and reliable test animal but it is even superior in many respects to other test animals such as the mouse and the rabbit. The reliability of the rat test in six hours enhances its value, particularly in the diagnosis of ectopic gestation or other acute abdominal conditions requiring surgical intervention. However, it must be strongly emphasized that considerable experience is necessary in reading the results of the tests in rats. All technical details must be properly attended to, and in all cases of doubt, the clinical history should be analysed and the test repeated. The number of comparative tests done is by no means large, but the data collected and the careful observations made would sufficiently warrant the inclusion of the rat in the group of test animals routinely accepted for pregnancy hormone tests. When depending on the results of six-hour rat test alone, not less than two animals should be used, one being killed after six hours and the other at the end of twenty-four hours. The value of such a procedure should be obvious.

Summary

The female immature rat having been shown to respond well to the anterior pituitary-like hormone in twenty-four hours, the test period

was reduced to two, four and six hours and the corresponding response was studied.

The six-hour test period was found to give results of sufficiently high accuracy and diagnostic value. On the basis of these observations, one hundred samples of urine were tested simultaneously with a six-hour rat test and Friedman test, using only one test animal. Ninety-six tests gave identical results. Indefinite reactions were obtained in three tests, and in one test the rat gave a false negative result. In no case was a false positive obtained by the six-hour rat test. The problem of indefinite reactions is discussed, and measures to prevent their occurrence are suggested. The use of at least two test animals is advocated when depending on the results of the six-hour rat test alone.

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A Mirror of Hospital Practice

PENICILLIN IN THE TREATMENT OF CARBUNCLE

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A CASE of carbuncle on the right shoulder extending over a big area, with slough and discharge, was admitted into this hospital on 30th September, 1945. No sugar was detected in his urine. The patient was in a bad state of health and it was decided to use penicillin. Twenty-five c.c. of a strength of 1,000 units per c.c. were injected all round and into the base of the carbuncle. The wound was dressed with penicillin and intramuscular injections of penicillin were also given. This treatment was repeated daily. The congestion subsided considerably and the slough partially separated after 24 hours and the discharge was also much less; after 48 hours the slough completely separated. The treatment was continued for another three days. No discharge was noticeable after the fifth day, and healthy

granulation started showing all round. The patient was discharged cured after two weeks.

Since that time I have treated about six cases of carbuncle in different sites with penicillin, and equally good results have been obtained.

RUPTURE OF ANEURYSM OF AORTA

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History of the case.—A Hindu male, aged about 35 years, visited a prostitute at about 9 p.m. on 6th May, 1944. He fell down unconscious on the bed of the woman in her room. He was taken out of the room and placed on the verandah where he died immediately after. No marks of injury or violence could be detected on the dead body. The body was subsequently sent by the police for post-mortem examination, as foul play was suspected. According to the statement given by the woman before the police, the man became suddenly unconscious just before the commencement of the act of coitus.

Post-mortem findings.—A fairly nourished subject. Rigor mortis was present. The eyes were partly opened, the pupils dilated and equal, conjunctivæ suffused. Cyanosis was present in the finger-nails.

On internal examination of the body, the following conditions were noticed :—

The heart was found enlarged, weighing 12 ounces. The right coronary artery was sclerosed. Both sides of the heart contained fluid blood. The ascending part of the arch of the aorta was markedly atheromatous. There was an aneurysm at the beginning of the aorta, which had burst into the pericardial sac. Thirteen ounces of clotted blood and 2 ounces of fluid blood were seen inside the pericardial cavity.

Both lungs were congested with some pleural adhesions. There were 4 ounces of serous fluid in the right pleural cavity and 2 ounces in the left side.

The stomach was congested and contained one pound of partly digested 'rooti' and vegetables.

The liver was enlarged 4 lb. 2 oz. and congested. The gall-bladder contained thin bile.

The spleen (8 oz.) was slightly enlarged.

Both kidneys (6 oz. each) were congested and enlarged.

The brain was slightly congested, so also were its membranes.

All other organs were more or less healthy.

Alcohol was found in the stomach and its contents, and only traces of alcohol were detected in the portions of liver and kidneys.

Discussion.—The immediate cause of death, in this case, was embarrassment of the action of the heart by accumulation of blood in the pericardial cavity, coming from a rupture of the aneurysm at the beginning of the aorta. Alcohol as well as excitement before sexual intercourse as was indicated by the statement of the woman concerned and presence of semen coming out of the penis might have been the precipitating causes.

Atheroma is a variety of arterial degeneration which affects and is almost confined to the intima and becomes more marked with advancing age. It is caused by chronic lead poisoning, gout, etc. Syphilis has no connection with atheroma. Again atheroma itself does not, as a rule, lead to aneurysm. But the atheroma may be associated with degeneration of the media, and in that case, a general dilatation of

the aorta is commonly seen. Circumscribed aneurysm may, however, also take place, though very rarely, from severe degeneration of the media.

A circumscribed aneurysm limited, as in this case, to the beginning of the aorta within the pericardial sac, seen more frequently in males, especially amongst hard manual workers, soldiers, sailors, etc., and in the 4th decade of life, is usually caused by severe medical degeneration from syphilitic inflammation.

Hence the sex, the age and the habits of the dead man, the site and type of the aneurysm and enlargement of the heart with coronary sclerosis, all lead one to think that the aneurysm of the aorta in this case was due to syphilitic mesaortitis causing weakening of the arterial wall.

CEREBRAL SYMPTOMS AFTER MEPACRINE *

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THE following case report appears of interest :—

A female, aged 20 years, had an attack of fever, and was admitted to the hospital on 13th March, 1945, with high fever. A blood film was examined, and tenuous forms of malaria parasites were found. The next day mepacrine one tablet twice daily was prescribed, preceded each time by an alkaline mixture. After taking four tablets of mepacrine, the patient developed peculiar symptoms, staring at the nurses, restlessness, and talking incoherently. She became violent and ran away from the hospital two or three times. She was brought back and kept under restraint, and an injection of morphine was given. Blood was again examined three days later, but no malaria parasites could be found.

The patient gradually became very violent and had to be kept under close restraint. She remained for four months in this condition, shouting all day and night, breaking panes and windows, and tearing clothes supplied to her. She then began to quieten down, and took another month to come to the normal state. She was discharged from the hospital on 6th September, 1945.

On enquiry no history of lunacy could be traced in her family.

Cerebral symptoms of a violent type developing during or shortly after the administration of only four mepacrine tablets, and lasting for a considerable length of time without being fatal, are striking points in this case.

A CASE OF LYMPHOPATHIA VENEREUM (LYMPHOGRANULOMA VENEREUM) IN BENGAL

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and

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A BENGAL male, aged 32 years, a clerk, came on the 22nd September, 1945, for treatment of buboes with

* Paper condensed by the editor.

multiple sinuses on both the inguinal regions and multiple granulomatous ulcers on the scrotum.

History.—Five months prior to entry in this clinic he noticed a slightly painful hard swelling, the size of a nut, on the right inguinal region. Gradually this became bigger and softer till in a month it burst with a discharge of sero-sanguineous fluid. A week after this the scrotal skin became swollen, inflamed and painful, and gradually ulcerated, with a foul-smelling serous discharge. The entire right side of scrotum was involved. About two months after the onset, another swelling of the same character, but bigger in size, appeared on the left inguinal region. This also became soft and burst with three distinct openings. There was a copious sero-sanguineous discharge; and the left side of the scrotum was gradually affected like the right.

A history of exposure was elicited, and the infection was probably acquired in the evacuee's camp in Assam.

The patient stated that before coming here he had the following treatment outside with no effect:—

1. Six intramuscular injections of sterodin (non-specific protein 2 c.cm. each).
2. A course of autogenous vaccine containing *Staphylococcus aureus*.
3. Sulphathiazole by mouth, 3 to 4 grammes only in about one week.
4. Acetylsarsan—three injections. Novarsenobillon—one injection.
5. Penicillin—one course 100,000 units.
6. Various local applications.

Present condition.—The entire scrotal surface was ridged with multiple fungating ulcers, granulomatous in appearance, pinkish red in colour. Tenderness, burning pain and a foul-smelling serous discharge were present. There were ten discharging sinuses, three on the left and seven on the right inguinal regions. The sinuses were painful, causing discomfort and the patient could not walk properly. The entire skin of the inguinal regions looked unhealthy and hyperpigmented here and there.

Investigations.—1. The total leucocyte count—12,000 per c.mm. 2. The Wassermann and Kahn tests were negative. 3. The Frei dermal test was positive in 24 hours and the reaction lasted for about a week.

Treatment.—The diagnosis of lymphopthia venereum being confirmed, sulphadiazine, three grammes daily, was given by mouth; on the fourth day a definite improvement was noticed; by the 8th day the fungating ulcers of the scrotum disappeared and the sinuses in the inguinal regions showed healing, some complete and some incomplete. On the 15th day healing was complete. The patient was asked to rest for one week and then have the same dose of sulphadiazine for another week. Seen after a month he was completely cured of the condition, with marked improvement in general health.

The points of interest in this case are: (1) lymphopthia venereum is rarely seen in this province; (2) the disease is quite common in Madras and South India, from where the labourers go to and from Burma; (3) the history of exposure in this case points to the infection having been acquired from a Burmese evacuee in Assam; (4) the prompt and complete cure with sulphadiazine alone.

A WASSERMANN-POSITIVE CASE OF PARALYTIC CHOREA

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DESCRIBED by Gowers in 1881 as paralytic chorea, this flaccid variant of chorea is not uncommon. It is a nervous manifestation of active rheumatism. Syphilis bears no relation to this disorder. The Wassermann reaction can become positive in a large number of diseases

apart from syphilis. The present case is one of paralytic chorea with a positive Wassermann reaction.

Case report

B., 10 years, Hindu male child, was admitted into the children's ward with the complaints of loss of power in the right upper and lower extremities, duration 10 days.

For one month he had been getting repeated attacks of epistaxis without any definite cause. Fifteen days before admission he developed fever lasting for 4 days. After the cessation of the fever, choreic movements appeared in his right upper extremity and lasted for 3 days. These movements completely subsided but were followed by loss of power in the same extremity. A few days later the right lower extremity also became powerless.

On examination.—The patient appeared well nourished and healthy. Temperature 98°F., pulse 92, respiration 22, blood pressure 92/62. Cranial nerves intact. Loss of associated movements in the right side, and presence of dragging of the right leg during locomotion. Right arm and leg showed diminished motor power, flaccidity, no wasting, intact co-ordination and sensations with loss of tendon jerks. Abdominal reflex present in all quadrants, and plantar reflex flexor. Other systems revealed no abnormality.

Investigations.—Blood: total red cells 3,760,000 per c.mm.; total white cells 4,000 per c.mm.; polymorphonuclears 49.0 per cent, lymphocytes 43.0 per cent, large mononuclears 4.0 per cent, eosinophils 4.0 per cent; hæmoglobin 11 grammes per cent. W.R. strongly positive, + + —.

Progress and treatment.—He was kept under rest and put on aspirin 5 grains thrice daily. A liberal diet was given. His mother's blood showed completely negative W.R. The boy gradually regained power in his right arm and leg. After two weeks his W.R. became positive, + ± —. After another two weeks his W.R. became completely negative, — — —. He was discharged cured.

Discussion

The interest of the case lies in the positive Wassermann reaction which became negative with the cure of the disease. The negative W.R. in the mother and absence of any stigma of syphilis in the boy were against the existence of congenital syphilis.

Acknowledgment

My thanks are due to Major-General H. S. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College, Agra, for his kind permission to publish this report.

A CASE OF 'AMCEBOMA'

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.), T.D.D. (Wales)

and

M. N. RAI CHAUDHURI, M.B. (Cal.)

(From the School of Tropical Medicine, Calcutta)

THE following case illustrates a form of amœbiasis which is perhaps not uncommon, and shows how it may lead to serious error in diagnosis and expose the patient to unnecessary surgical operation:—

A Bengali male, aged 44 years, was admitted to the Carmichael Hospital for Tropical Diseases, Calcutta, on the 4th February, 1946. His

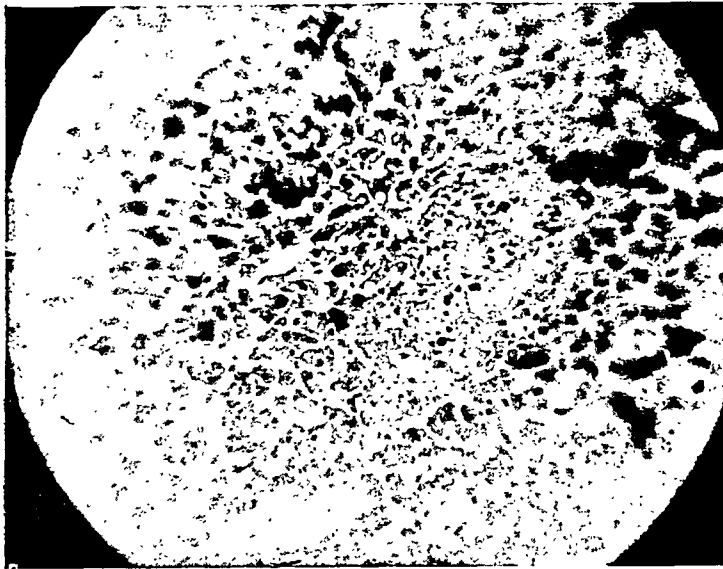


Fig. 1. Case 1.—Subacute hepatitis.

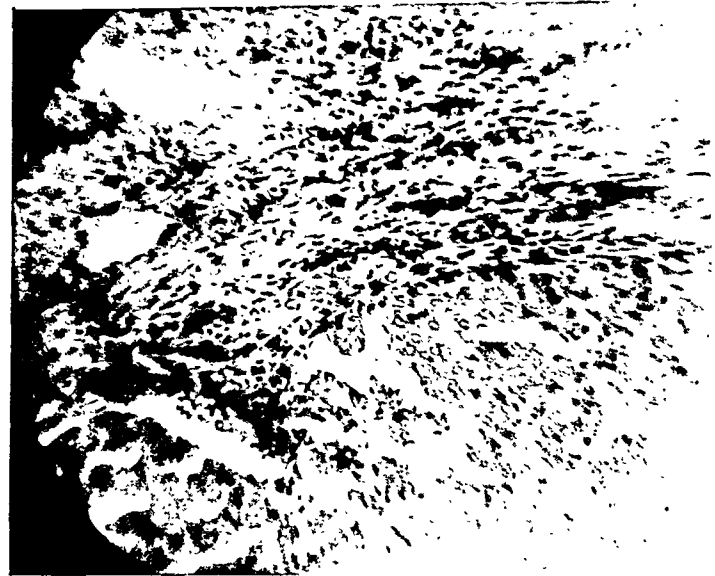


Fig. 2. Case 2.—Hepatic cirrhosis. Well-marked cirrhosis with fatty changes in hepatic cells.

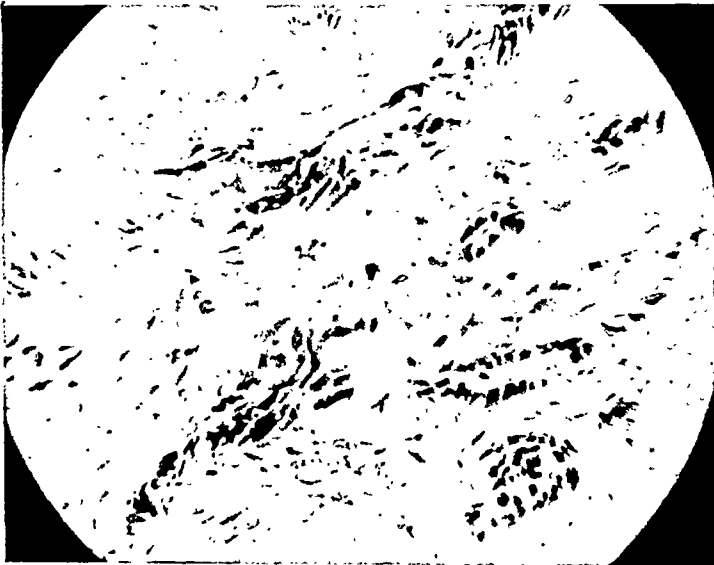


Fig. 3. Case 3.—Adenocarcinoma.

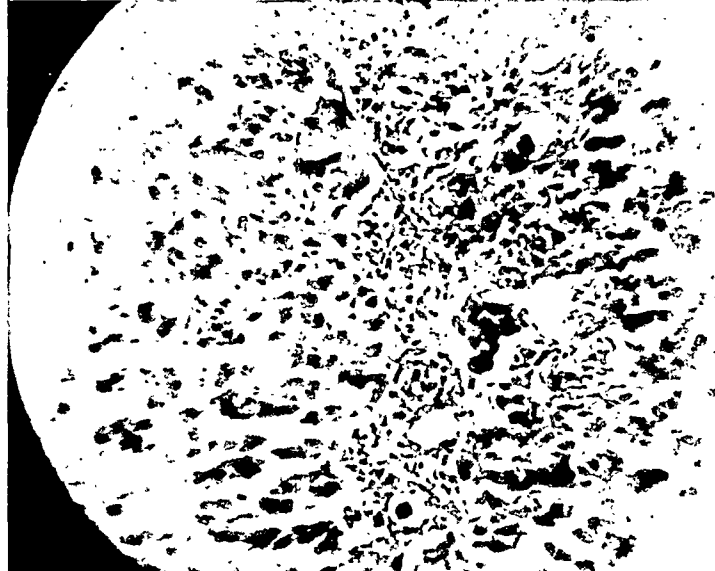


Fig. 4. Case 4.—Hepatic biliary cirrhosis.



Fig. 5. Case 5.—Primary cancer of the liver.

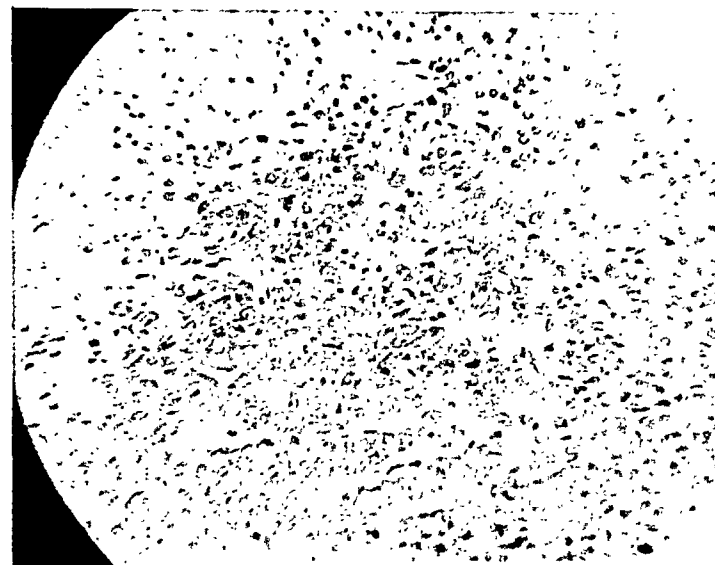


Fig. 6. Case 6.—Extra hepatic biliary obstruction.

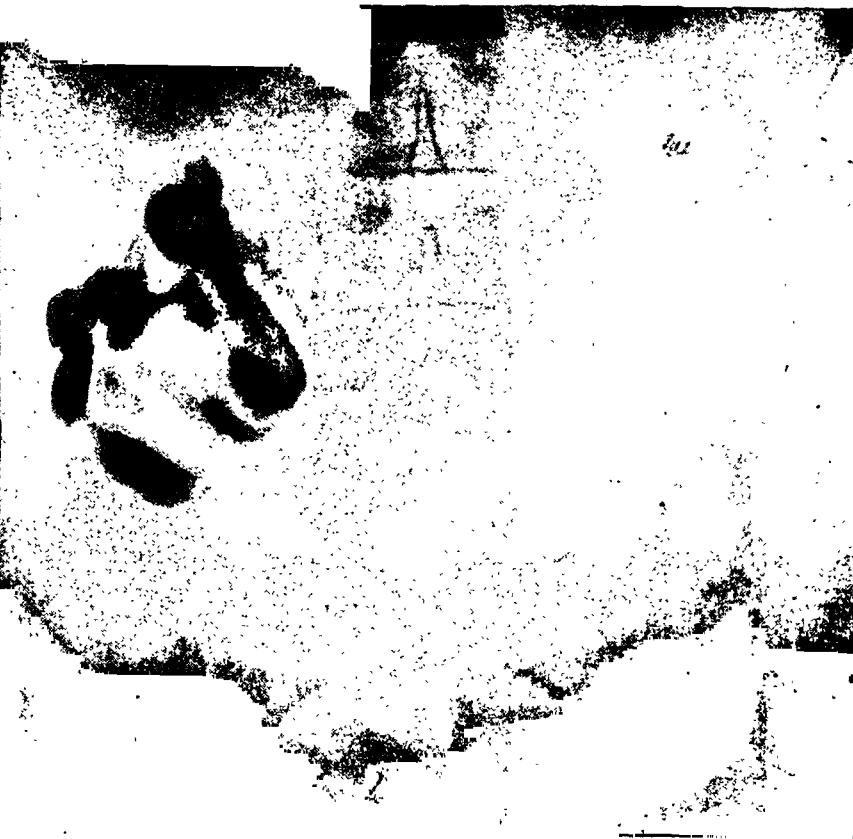


Fig. 1.—Irregular residue in the caecum after 24 hours.



Fig. 2.—Defective filling of the caecum even after half an hour.



Fig. 3.—Well-defined caecum with barium enema after treatment.

symptoms were fever, abdominal pain, and diarrhoea, duration one and a half months. He also complained of a lump in the abdomen which had been existing for about six months.

The history was that he had suffered from dysentery for two months in 1944 and from fever for five months in 1945. Thereafter, the abdominal lump appeared; it began as a small swelling in the right iliac region. There was a considerable loss of weight, about 3 stones in 1½ years. His doctors suspected the condition as tuberculous caecum with localized adhesive peritonitis and advised short-circuiting.

On examination, the mass was 4 inches by 2½ inches; it was firm, irregular and tender, obviously involving the ascending colon and right half of the transverse colon. No other abnormality was detected. The white cell count was 10,000 with 80 per cent polymorphs. Other laboratory tests were negative. Barium meal examination revealed an irregular residue in the caecum after 24 hours (figure 1, plate XIV), while the barium enema showed a defective filling of the caecum even after half an hour (figure 2, plate XIV). X-ray examination of the chest showed no lung infiltration.

After the x-ray examination, the distal portion of the 'tumour' mass disappeared, and it was attributed to emptying of the transverse colon as a result of purgation and enema. The lateral portion however remained unaltered, and we thought that this might be due to amebic granuloma of the caecum and ascending colon. The patient was put on emetine (grain 1 daily for 6 days), and carbarsone (0.25 gm. twice a day for 10 days) empirically, which not only relieved his symptoms but led to the complete disappearance of the 'tumour' mass. He has now put on 9 lb. in weight within a fortnight, while his haemoglobin increased from 8.8 gm. to 9.9 gm. Another skiagram taken almost immediately after barium enema showed a more well-defined caecum (figure 3, plate XIV).

In differential diagnosis, one may think of tubercle, cancer, faecal impaction and collection of roundworms, but the rapid response to emetine supports the diagnosis of 'ameboma', although undoubtedly there was some chronic accumulation of faecal matter in the colon.

ENLARGED PROSTATE TREATED WITH STILBOESTROL

By S. M. SADIQ, M.B., B.S.
Panipat (Punjab)

THE operative mortality even in expert hands is so high and the undertaking of operation in the districts is so risky that one contents oneself only with the relief of symptoms in this disease. I have tried all sorts of medical treatment and even the simple operation of Steinach's vasectomy but without any marked benefit. Last year, a suggestion came from the inspector-general of civil hospitals, Punjab, to try stilboestrol tablets. Since then I have tried these on eleven patients with good results specially in early cases. I have not been able to judge about the benign or malignant types, but the fact remains that some cases were very advanced and toxæmic and failed to respond altogether. It may be that I could not give a fair trial as the patients left the hospital; moreover, the cost is prohibitive for some patients. The following are brief notes on some of the cases treated with stilboestrol.

Case 1.—Patient aged 67, frequency of micturition at night and an urgency since about two months. Rectal examination revealed enlarged prostate. Put on stilboestrol tablets, one three times a day. Felt better within a week. Advised to carry on with the same treatment with one tablet daily. No frequency of micturition at night now.

Case 2.—Early case. Patient aged 59, similar to case 1, and similarly treated. Got better after 8 or 9 days and also has been well for the last year.

Case 3.—Patient aged 55, had retention of urine twice; considerable difficulty in passing urine. Relief with treatment, but came again with retention, looking very weak and toxæmic. This time there was no improvement.

Two other cases had stones in the bladder which were removed by litholapaxy. The prostatic symptoms in one of them did not improve until I started giving injections along with oral medication. The record shows that out of the eleven cases two did not respond to treatment, one responded partially, but the remaining eight were completely relieved. I cannot deny that the symptoms of these patients do sometimes subside after treatment with catheterization, etc., but the first two cases are rather instructive; these have remained symptom-free and another patient gets back his urinary troubles only if he is not given stilboestrol injections regularly.

TREATMENT OF ECLAMPSIA WITH MAGNESIUM SULPHATE

By M. A. QUDDUS, L.M.F.

Chamta Dispensary, P. O. Niamoti (Bengal)

A FEW years ago the district health officer of Backerganj circulated a pamphlet suggesting magnesium sulphate injections for the treatment of eclampsia. Roy (1941) treated some cases with intravenous injection of 15 c.cm. of 10 per cent solution of magnesium sulphate, along with Stroganoff's treatment, intravenous glucose, etc. I have treated 15 cases of which only two died. In all these I injected 5 c.cm. of 25 per cent solution of magnesium sulphate intramuscularly, followed by an injection of morphine ¼ grain and atropine 1/80 grain. The fits and convulsions stopped after these two injections, and the patient fell into a deep sleep. In 9 cases there was no recrudescence of the symptoms; in 4 they reappeared after 3 hours and were stopped by another injection of 5 c.cm. of magnesium sulphate solution. All the cases were ante-partum and a dead child was delivered in each case 8 to 10 hours after the commencement of treatment. The two fatal cases were completely unconscious and cyanosed; fits were coming in quick succession and respiration was hurried. An intramuscular injection of 10 c.cm. of magnesium sulphate stopped the fits and convulsions, but the patients died within an hour.

In January 1946 I treated two more cases by the above method, one a primipara aged 16 years and the other a multipara aged 35 years. The fits and convulsions stopped, and the patients regained consciousness, and after 8 to 10 hours the dead child was delivered spontaneously. Both cases recovered uneventfully.

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A CASE OF RUPTURED UTERUS

By D. PARANJOTHY, M.B., B.S., D.G.O., D.T.M.
Christian Hospital, Azamgarh

A MOHAMMEDAN female, aged 25, third para, was admitted to the hospital on 10th October, 1945, at 7 p.m., giving history of labour pains since early morning.

The first delivery was normal and full term; the child is still living and is six years old. The second delivery was contra placenta prævia; the patient came to hospital in a collapsed condition after having bled for 24 hours. Classical Cæsarean section was done; premature baby, still-birth. She was discharged six weeks later after a stormy and prolonged convalescence.

About a month ago the patient came for antenatal examination, at 36 weeks. The external pelvimetry was: I.C. 9½ inches, I.S. 9½ inches, E.C. 7 inches. Blood pressure was 125/95, and the urine was clear. The patient was admitted for treatment for anæmia. Advice was given that a normal delivery could not be expected and that she should be brought early for an abdominal operation. The patient left the hospital before the treatment was completed and nothing more was heard of her till her present admission. The husband stated that the patient had become unconscious in the afternoon, her condition gradually became worse, and that *dais* and doctors had examined her.

On admission, the patient was very restless and complaining of epigastric pain; pulse 148, very weak; temperature 98°F.; tongue very dry; foetal heart not heard. The patient was given coramine and sub-mammmary saline and prepared for Cæsarean section, but owing to factors beyond my control, I could not attend until 1 a.m.

The patient was still restless, breathless and scarcely able to articulate, and tender. Abdominally the uterus appeared tense and rigid and the foetal part could not be made out. Per vaginam the cervix was just felt very high up behind the symphysis, but neither the dilatation nor the present part could be made out. An hour later, the abdomen was opened under general anæsthesia by sub-umbilical median incision. The uterus had ruptured completely at the previous Cæsarean scar and the baby and placenta were lying in the abdominal cavity. Suturing seemed inadvisable. A rapid hysterectomy was done and the abdominal cavity swabbed with sulphonamide powder and the abdomen closed in layers.

The patient's condition became very low. Morphine and rectal saline were given, but the low state continued. Coramine and two soluseptasine injections were given. She slept fairly well on morphine, but in the early morning was troubled by distension which was relieved by flatus tube. Eserine followed by turpentine enema had also to be given subsequently. Next day, blood examination showed total red cell count to be 0.7 million per c.mm. and hæmoglobin 25 per cent. Arrangements were made for blood transfusion and 250 c.cm. of whole blood were given on the following day. On the 7th day, soluseptasine injections were stopped and oral administration of sulphanilamide tablets was started. The total red cell count rose to 2 millions and the hæmoglobin to 45 per cent. Another transfusion, 500 c.mm., was given on the 11th day followed by a more marked reaction. Three days later the total red cell count rose to 2.7 millions and the hæmoglobin to 60 per cent. After another two days, the temperature came to normal and continued to be so. She was discharged six days later; the total red cell count at the time of discharge was 3.5 millions and hæmoglobin 70 per cent.

Comment.—This case is of special interest to obstetricians working in backward areas where mothers come to hospital only after all the *dais* have failed to produce the desired result. We get about 70 cases for delivery annually of

which 60 per cent are abnormal, and in the last 441 cases 20 had ruptured uterus. In the case under report, it seems that the uterus must have ruptured very early in the morning and until 7 p.m. on the day following she had no medical treatment. This itself would have made a poor prognosis for her, but besides that she had to wait 7 more hours until my return for the operation. It is therefore clear that laparotomy should be done in such cases provided the patient's condition is reasonably good.

AFEBRILE CASE OF ACUTE MILIARY TUBERCULOSIS OF BOTH LUNGS

By B. L. CHOPRA

Divisional Medical Officer, N.-W. Railway, Ferozepore

A Loco turner, about 40 years old, was admitted to this hospital on 4th December, 1945, with cough and expectoration, hoarseness, and also loss of weight for the last four months. These symptoms were very marked during the two weeks preceding admission.

The examination of the chest showed a few scattered medium-sized crepitations with slight impairment of the percussion note. The heart, spleen and liver were normal. Repeated examination of the sputum showed no acid-fast bacilli. The blood examination showed a low total red cell count of 390,000 per c.mm., and hæmoglobin 62 per cent, but no other abnormality. The total white cell count was 7,000 per c.mm., with 63 per cent polymorphs, 32 per cent lymphocytes, 4 per cent large mononuclears, and 1 per cent eosinophils. The man showed no rise of temperature and no active signs of lung disease; an x-ray photograph of the chest was taken. The skiagram showed mottling of both the lungs suggestive of milary tuberculosis.

The patient stayed in the hospital for ten days and never showed any temperature whatsoever during this period.

SULPHONAMIDE ANURIA

By T. N. RAI

Windham Hospital, Jodhpur

A MOHAMMEDAN male, aged 15 years, was admitted to the surgical ward of this hospital on 29th December, 1945, for osteomyelitis of the right leg. A course of sulphonamide two tablets thrice daily was prescribed and the leg was operated on. Ten days later he showed signs of pain and fullness over the back and loin, and there was complete anuria. Sulphonamide was at once stopped, and alkaline mixture and plenty of fluids, a hot water bath, a soap and water enema, and fomentations over the loins were given. The bladder was catheterized but there was no urine. Intravenous glucose saline also gave no relief. The pain continued, and the patient became weak and prostrated. Cystoscopy and ureteral catheterization were done and the catheter was tied in. During the next twelve hours the patient passed about 24 oz. of urine and continued to pass urine. The urine showed the presence of red cells and some albumin but no other abnormality. The symptoms gradually subsided.

(Sulphonamide anuria has been very rarely reported in India. This is surprising, since with high temperature and profuse sweating, and with limited fluid intake, the concentration of sulphonamide in the kidney tubules might be expected to rise high. In the case here recorded, the dosage of sulphonamide was low, but the period of administration was long. It is not stated what sulphonamide was given.—EDITOR, I.M.G.)

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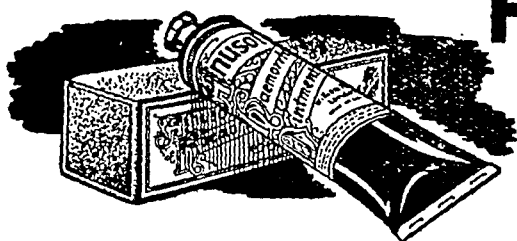
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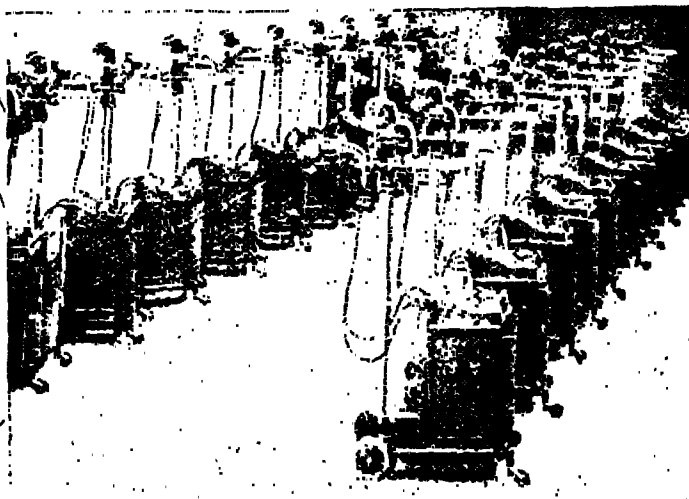
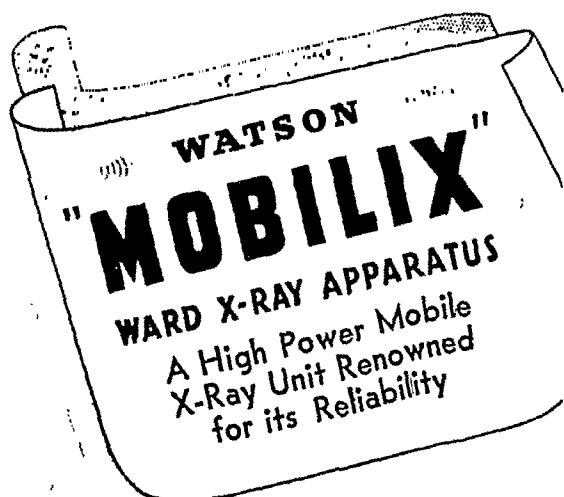
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Indian Medical Gazette

MARCH

THE Rh PROBLEM IN INDIA

THE Rh hæm(agglutin)ogen in the human red blood corpuscles (rbc hereafter) was discovered 5 years ago (Wiener and Landsteiner, 1941). Almost immediately afterwards its relationship to erythroblastosis foetalis was traced (Levine, 1942). It also explained why when incompatibility of groups, dangerous universal donor and even incompatibility of types were excluded, blood transfusions at times not only did not improve the blood state of, but actually killed, the recipient.

The hæmogen is found normally in the rbc of the Indian brown monkey, *Macacus rhesus*: the Rh are the first two letters of the specific name.

A rabbit (or a guinea-pig) injected with the rbc of the monkey develops in its blood an antibody against the Rh and supplies the animal serum for testing human blood. In certain dilutions the serum agglutinates the rbc of a certain proportion of human subjects. These subjects are Rh +. Those whose rbc are not so agglutinated are Rh -.

Another source of the testing serum is an Rh - mother who has carried an Rh + foetus. She has become *iso-immunized* with the rbc of the foetus, which have strayed from its circulation into hers. The iso-antibody formed by the mother damages the rbc of the foetus: hence the disease. The foetus may be cast off as an abortion or delivered as a diseased infant suffering from jaundice and dropsy in various degrees. Such a mother (or expectant mother) comes to grief herself if transfused with Rh + blood. Those connected with the pre Rh blood transfusion schemes and blood banks knew that unexpected accidents occurred more often in maternity cases than in other cases.

In a male Rh - recipient the transfused Rh + rbc also iso-immunize the patient and are destroyed more or less speedily: the case is not benefited. After a second transfusion from the same donor (or another Rh + donor) the male recipient comes to grief like the Rh - mother.

The figures for the Rh + and Rh - subjects vary with the race. Amongst the Europeans they are of this order: Rh + 85 per cent, Rh - 15 per cent. Amongst Indians they became available in 1943 in Calcutta and were of this order: Rh + 90 per cent, Rh - 10 per cent (Greval and Roy Chowdhury, 1943). They were confirmed in Calcutta in 1944 (Das Gupta, 1944). They were contradicted in Bombay in 1945 (Khanolkar and Sanghvi, 1945). They were confirmed again for the Punjab (by examination of sailors) in America (Wiener,

1945). The Rh - rate may be taken to lie between 7 per cent and 10 per cent, roughly about half of the European Rh - rate.

Dangers of the incompatibility of the Rh state are two: (1) Accidents of blood transfusion. The risk in married females is higher in as much as the accident may occur in the first transfusion. When only an animal serum is used in the test many reactions are 'doubtful' (\pm). They are taken as positive (+) in determining the Rh state of a subject. But in a recipient they should be taken as negative (-) and an Rh - donor provided. (An Rh - donor does not harm an Rh + recipient.) Further, a very small proportion of Rh - subjects found to be negative by animal testing serum may be positive (Rh' and Rh'') by human testing serum. Special care is, therefore, necessary in cross matching the blood of married females. The accidents, though most likely to occur during pregnancy and after parturition, may occur after an abortion and long after the child-bearing age. The Rh - males transfused with Rh' and Rh'' blood (which will be returned negative by animal serum) will not benefit by the first transfusion. The accident, however, will occur only with the second transfusion and can be prevented by a careful cross matching of bloods. Weak agglutinins can be detected by the use of anti-human-globulin serum (Coombs, Mourant and Race, 1945). Absolute safety can be guaranteed after a biological test in which a sample of the donor's blood is injected into the recipient and one hour later a sample of blood is drawn from the latter to see if the serum is tinged with hæmoglobin (Wiener, Silverman and Aronson, 1942). If the serum is not tinged, a previously sensitized male, an expectant mother or a mother can be safely transfused from the donor. Safety of the foetus, however, cannot be guaranteed when the test is undertaken for the benefit of the mother. The small quantity of the incompatible blood used in the test may raise the titre of the mother's anti Rh serum and increase the damage to the foetus. The danger is less in India in proportion to the lower Rh - rate but is not negligible. Incidentally, intragroup and anomalous reactions unconnected with Rh hæmogen are known to be given by pregnant women. Besides, anti Hr and St sera from Rh + expectant mothers have been described. They agglutinate Rh - or heterozygous Rh + rbc (McCall, Race and Taylor, 1944). (2) Erythroblastosis foetalis (and consequent abortions and sterility). The disease does not appear to occur in India. In Calcutta the Imperial Serologist's Laboratory has been in touch with all maternity hospitals since 1943 and has not yet contacted a case. The same observation has been reported from Bombay. The reason may be some subtle tellural influence or a lack of chilling. The latter is suggested by paroxysmal hæmoglobinuria which is rare in Calcutta and depends on chilling solely.

The genetics of the Rh state was very simple in 1941, the two genes being (i) dominant Rh and (ii) recessive rh. The position at present is complex and far from steady. The Rh is divided into Rh₀, Rh₁, Rh₂, Rh' and Rh'' and a few more Rh's, besides. Mathematical prophecies (Fisher, quoted by Coombs, *loc. cit.*) threaten to lengthen the chain. Antibodies are represented by many Greek letters, and a serologist approaches his test tubes or slides with fear and trembling. Forensic application, obviously, would not be safe at present. Interference with clinical application is slight and can be mostly guarded against.

Incidentally, Rh is a *character* genetically and an *antigen* immunologically: the term *factor*, loosely, is not really necessary.

S. D. S. G.

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STETHOSCOPE VERSUS X-RAYS

It is a remarkable fact that in the midst of advances and discoveries that have occurred during the last century the stethoscope has maintained a place that is almost unrivalled by any other weapon in the medical armamentarium. There are quite good reasons for this popularity, for no other single instrument can give so much information about two of the vital organs of the body. It is the doctor's hall-mark, and no visit to a patient, even when he is a doctor himself, is considered complete unless the chest is 'sounded', although his illness may have nothing to do with this part of his body. So it is not surprising that when x-rays came to be used for diseases of the chest there were physicians who would not admit its superiority over the stethoscope. The difference in opinion lay chiefly in the diagnosis of pulmonary tuberculosis, and here they claimed that they could detect the disease in its early stage by physical signs, even before the sputum became tubercle positive. The radiologists retorted by saying that the absence of these signs did not exclude tuberculosis, and that at this stage x-rays alone

could be of real help. It must be admitted, however, that the radiologists were partly responsible for the physician's attitude, for in the past they were often prone to pronounce any shadows in a skiagram as tuberculous with the result that many a person had unnecessarily to leave his occupation and lead a shattered life. Sometimes they have gone to the other extreme of reporting healing or inactivity of a lesion on insufficient grounds. With the growth of experience, less dogmatism now prevails, but there are still physicians who fail to appreciate that while physical signs mean disease, the reverse is not true, and there are radiologists too who are not free from the faults we have just mentioned.

Although the detection of tubercle bacilli is more precise than any other method of diagnosis, the superiority of x-rays in pulmonary tuberculosis has led some physicians and radiologists to assert that the stethoscope is now not so important as it used to be in the past. This is only partly true for which our teachers are somewhat responsible for they still lay too much stress on insignificant signs, and multiply labels to the various sounds heard through the stethoscope, so that the student gets a false sense of their value and is inclined to assume that disease is not present when auscultation is negative. Its effect is nowhere more disastrous than in pulmonary tuberculosis in which radiological signs are usually the earliest to appear often with such vague symptoms as lassitude, 'dyspepsia', repeated catarrh or irritant cough. Diagnosis at this stage is too often delayed because some prefer to wait for stethoscopic signs or even positive sputum. Radiology is also superior in occupational fibrosis, cancer and cyst of the lung. But physical examination, apart from its psychological effect on the patient, has still an important place in diseases of the chest. X-rays are inconvenient in acute cases, and they do not disclose anything special in bronchitis, bronchial spasm or dry pleurisy. An early bronchiectasis may not reveal itself on a straight x-ray picture, but is more frequently apparent on stethoscopic examination by the presence of persistent localized râles especially at the base. The presence of added sounds is of immense importance where an indifferent skiagram fails to reveal disease, and can also yield strong presumptive evidence of activity in cases of tuberculosis which radiologically appear to be healed.

At a recent debate in the Royal Society of Medicine, in which both physicians and radiologists participated, it was generally agreed that while in cardiology the stethoscope still reigns supreme, it has reached its limits in chest diseases and that these limits are so narrow that radiography is indispensable. But it is by no means, as an experienced radiologist said, an obsolete instrument. One physician remarked that if he had to choose between two instruments, it would be the x-rays every time although he

would be very sorry to be without the stethoscope as it might be a very useful adjunct. There is no doubt that radiography is invaluable in three groups of cases: where there are no physical signs, where physical signs are present but their significance cannot be decided without radiology, and where diagnosis could be made with certainty on physical signs but the extent of the disease could be shown only by x-rays. In children physical signs of pulmonary disease are often indefinite, and radiology can give better information than the stethoscope. But x-rays have limitations too. Slight errors in technique may produce confusing results. A straight view sometimes fails to show cavitation of the lung, and radiologists are not always able to explain abnormal appearances. There are also some rare cases in which physical signs may reveal disease not apparent upon the skiagram even when it is examined by an expert. Probably more methodical use of lateral and oblique views and also of tomography would reveal many hidden lesions, though such a procedure would be very costly. It needs to be emphasized that x-ray film, to be of value, must

be a good one, and to express an opinion on an indifferent film as a guide to diagnosis is worse than useless, and it must also be remembered that the value of the method depends ultimately on the knowledge and experience of the man who interprets the appearances.

Finally, we may point out that the value of physical examination must not be minimized, and x-rays should not replace it. The present order of examination—history, physical examination and radiology—should be retained, and the physical signs and x-ray appearances should be considered together and carefully correlated. It is worth emphasizing that suspicious symptoms always warrant an x-ray examination though there may be no suspicious signs, but often it is not done for a variety of reasons of which may be mentioned lack of facilities, poverty and fear in case something serious is discovered. Sometimes the attending physician himself fails to advise an x-ray examination in circumstances where these questions do not arise; this is a serious omission which exposes him to the charge of negligence.

R. N. C.

Special Article

SOME PROBLEMS OF MEDICAL AND GENERAL INTEREST*

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Tendency towards irrational therapy.—In the course of my Presidential address to the Medical and Veterinary Section of the Indian Science Congress in 1927, I remarked that the number of members of our profession in this country who made use of drugs in an irrational way was surprisingly large. In ancient times, therapy was empirical because the aetiology and pathology of disease were not thoroughly understood, and our diagnostic methods were limited. During the last thirty years remarkable advances had been made in these branches, and therapeutics has been emerging from empiricism, and is now based on clearer conceptions of aetiology, physiology and pathogenesis. Unfortunately, the non-critical and indiscriminate use of drugs is still prevalent in spite of this advance in our knowledge. One has only to look at most of the prescriptions written by practitioners in India to see the true state of affairs. There still persists great temptation to write 'shot-gun' prescriptions, as well as to advise the use of all kinds of novelties introduced from time to time and which survive

only for a year or two in the drug market. Proprietary medicines, the composition of which was not known, are commonly prescribed, and different kinds of patent foods are advised, when simpler and very much less costly remedies of equal value are available. Many kinds of digestive ferments and glandular products are included in prescriptions though they are frequently inactive, especially in India where they are so readily liable to deterioration. Vaccines and sera are injected without due regard to their utility in the conditions under treatment. Amongst the lay public there is a craze for the administration of drugs by the intravenous or intramuscular routes, and the idea seems to have gained ground among medical men that drugs were only effective when given in this manner. Then again, any drug advertised in a medical journal is considered to be useful if backed by 'testimonials'. It does not appear to be realized that in addition to a large number of useful and potent drugs on the market there must have been a host of others of doubtful value.

Too much drugging.—These observations were made 18 years ago, and during the long years that have passed, one would have thought that this state of affairs would have improved. Unfortunately improvement, if any, has been very small. There is still a marked tendency on the part of the medical practitioners to overdose their patients with drugs, and thus an enormous amount of money is wasted on medicines of doubtful efficacy. Patients for whom

* Being an inaugural address to the 22nd All-India Medical Conference held at Amritsar in December 1945.

no specific treatment is available are dosed with complicated mixtures of expensive medicines, when attention to diet and other forms of general treatment, such as proper nursing and care of the sick and convalescent, would do more good than all the medicaments known. The public in this country have a child-like faith in medicines to cure all their ills and medical practitioners are often too complacent to encourage this idea. This has considerably lowered the status of medical practice.

Medical education.—One important cause leading to lowering of the status of medicine in India is the defective system of education. It is a source of great satisfaction to most of us that the method of training two grades of medical practitioner is rapidly coming to an end. It is completely finished in this province, and I hope it will soon finish in others. Every effort should be made in this direction. Many of the medical teaching institutions, however, are still poorly equipped and inadequately staffed. The pernicious system of allowing the teaching staff to carry on private practice has led to abuse, the far-reaching effects of which are now being fully appreciated. It is impossible for the teachers to have large private practice and at the same time to perform their instructional duties in a satisfactory manner. In America and many of the European countries, the evils of this system were recognized long ago and whole-time teachers were employed. The advantage of this procedure is obvious; the professors and teachers, being free from the anxieties of having to earn the whole or a part of their living by private practice, devote themselves entirely to their subjects, and come in closer instructional contact with their students. They also get time to devote themselves to scientific research in their subjects. One of the chief reasons why medical colleges in India have participated so little in the carrying out of medical research, especially on the clinical side, is the pernicious system above referred to and which unfortunately is still in general vogue. The Health Survey and Development Committee fully discussed this question, and it is hoped that in the future planning of medical education this evil will be eradicated.

The medical curriculum.—Then again, the medical curriculum in this country is still far from being satisfactory, though improvements have been made during recent years. The course is still overcrowded, and the student is burdened with too many subjects and too much detail which confuses his mind. There are far too many lectures giving information of the kind which a student can pick up in any textbook. The teachers have not the time to read up recent literature, and to present the great mass of theory and knowledge to the students in a carefully prepared, systematic and concise form, so as to enable them to grasp the essential facts and understand how to utilize the

detail in actual practice. Practical instruction also needs considerable improvement. A lot of unimportant detail is taught which is of no use to the medical practitioner.

The teaching of pharmacology, the science of action drugs, which forms the basis for treatment of disease, needs considerable improvement. Though diagnosis is of prime importance, the patient is less interested in it than in the treatment of his disease. To state that the future of medicine lies in pharmacology may seem fanciful, but there seems to be little doubt that the progress of medicine to-day is to be found in the progress of the science of treatment.

Little or no research work is carried out in many of the teaching institutions in this country, and students do not get into the habit of thinking independently of the views expressed in their textbooks. This affects their future careers as medical practitioners in an unfavourable manner, as they are always likely to believe what they see in print. Every teaching institution worth the name should have a department of experimental medicine, with a clinical research unit, where students can see and feel research work carried out in different branches of medicine including experimental therapeutics.

Drug control legislation.—One of the serious handicaps from which the medical practitioner suffers in this country is lack of control in connection with the drugs in the market. Although the Drugs Act was passed in 1940, the machinery necessary to give effect to its provisions has not yet been implemented. The result is that even now there are no safeguards whatever against manufacturing, advertising and selling to the public, of therapeutic products of any kind, whether potent or inert, effective or ineffective. Many of the preparations, both proprietary and otherwise, which are presented for sale are not up to the standard. It is gratifying to note, however, that rules and regulations in connection with drug control have at last been approved by various provincial governments, and the machinery of control will soon be functioning. The present legislation, though far from being perfect, especially with respect to advertising, will have a very great effect towards stabilizing the quality of drugs on the market.

It will be remembered that an important recommendation of the Drugs Inquiry Committee (1930-31) was that the drug control legislation and legislation for the control of the profession of pharmacy should be enacted simultaneously. Although this was not done, the Government of India realize the importance of such a measure, and legislation to control the profession of pharmacy will be one of the first items to be put through the new Central Legislature.

Medical relief.—It is well known that the illnesses of less than 25 per cent of the population in this country are located by scientific

medical practitioners. One reason for this is that the dispensary facilities and hospital accommodation are entirely inadequate for the needs of the large masses of population. Dispensaries and hospitals are generally few and far between. Hospitalization is essential for the efficient treatment of many diseases, and in most of the countries in the West, provision of ample hospital accommodation exists and this is of immense help to medical practitioners. Such facilities are utterly lacking except perhaps in a few of the large towns.

It has been estimated that 4.5 beds are required per thousand of population for sick and chronic cases. In actual practice, in more advanced countries, the figure ranges from 1.5 in Japan and 5.3 in Great Britain to 5.8 in Sweden. In India the number of hospital beds of every description, including mental hospitals and leper asylums, available for the population in 1937 was 0.3 per thousand, and probably this figure is not much higher now. The number of medical men and nurses available is also very low. There is undoubtedly a pressing need for improvement in this unsatisfactory situation.

Incurables.—Something should be said here about the care of people suffering from chronic type of incurable diseases, who go on suffering and lingering for prolonged periods. A large group of such patients are permanently incapacitated from earning a livelihood, and need the active care of the community in general and medical profession in particular. In other countries, much has been done to decrease the number of incurables by the proper application of the discoveries of medical science and to make the life of those suffering from these affections less miserable and more contented. In this country no organized effort has been made so far.

The cost of drugs.—The cost of drugs is so high in relation to the low economic condition of the people that there are millions of people who cannot afford any kind of treatment, whether cheap or expensive, and have to consequently depend upon charitable relief institutions. The cost of drugs is so heavy that most of these institutions which have limited funds for drugs and which have to cater for a population ranging from 10,000 to 100,000 spread over many square miles, are not able to cope with the demand for even the most essential drugs, to say nothing of expensive medicines which are sometimes required.

Use of indigenous drugs.—The only way in which the drugs can be cheapened and brought within the means of the masses is to utilize the local resources and use indigenous products instead of expensive imported preparations. This can be done by encouraging the production, cultivation and manufacture of the local drugs in a systematic manner. By local production and the use in treatment of potent drugs of Indian origin, the cost of treatment of ordinary

ailments which form the majority, can be considerably reduced.

The research in indigenous drugs which has been financed by generous grants from the Indian Research Fund Association, Council of Scientific and Industrial Research and Imperial Council of Agricultural Research has done much towards the development of the drug industry in India and towards encouraging the use of raw materials produced in the country for the preparation of galenical and other preparations. The objects of this industry should be twofold : (i) to make the country self-supporting so far as medicaments of every description are concerned; and (ii) to produce drugs economically so that they fall within the means of the people of India, whose economic condition is very low.

An Indian pharmacopœia.—Studies carried out on Indian indigenous drugs are gradually paving the way for the preparation of an Indian pharmacopœia. A national pharmacopœia is primarily meant to meet the claims and satisfy the needs of a particular group of medical men and patients at a particular time. The modern pharmacopœia is a book of standards and usage, rational usage and scientific usage. The time-honoured principles of the medical profession have been that there should be no secrets about drugs used in the treatment of disease.

The importance of the compilation of an Indian pharmacopœia cannot be overrated. Considerable work, however, must be done in working out our own standards, with due regard to climatic and other conditions, and the standardization of raw materials from which medicinal drugs are prepared, before this can be accomplished. It is very gratifying to note here that at last a beginning has been made and the Committee appointed by the Government of India has submitted a comprehensive report including a large number of indigenous products which will provide the first step towards the preparation of an Indian pharmacopœia.

The medical and public health services.—Before I stop I wish to say a few words about the organization of the medical and public health services in India. Under the conditions prevailing in this country, the State is essentially responsible for curative and preventive medicine. These two services are at present practically working in two watertight compartments. This is against the modern trend in advanced countries. Curative medicine forms an integral part of the public health services of a country, in as much as very often a sick man is the source of infection and no constructive medicine is possible unless the population is rendered free from disease by treating individuals. Again according to the newer conception of a State, it is necessary that disablement, whether temporary or permanent, should be cut down to a minimum through the intensive use of curative measures. Moreover, it is through curative medicine alone that it is possible to win the confidence of the public in a country like ours and bring home to

the people the advantages accruing both from preventive and constructive medicine.

Starting from the bottom, I consider that, to meet the requirements of public health in India, there should be a combined establishment which should form the basis of preventive, curative and constructive medicine in each village. This should be linked up with a more organized central agency, discharging these combined duties, catering for a convenient sized population, the bulk of which will depend on various factors such as communications, incidence of disease, etc. These primary centres would be linked up with district centres, with a more specialized staff, and these latter with the provincial organization with specialists in various branches of medical science. The head of this organization should be an experienced medical man with a thorough training in the methods of public health administration, community health organization, constructive medicine, etc., who will work under the Provincial Ministry of Public Health. The activities of provincial health organizations should be co-ordinated by an elaborate and efficient federal all-India organization under the Federal Ministry of Health. Curative and preventive medicine must work as a single whole. To let them work separately would only lead to confusion.

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[With nearly everything that Sir Ram Nath says we are in close agreement. The only real disagreement is on the question of indigenous drugs. Sir Ram Nath thinks that some indigenous drugs are effective and cheap, but they are not prepared scientifically and standardized. We believe that there is no Indian indigenous drug that cannot be replaced by a more effective modern drug, and that indigenous drugs are not highly effective by modern standards. Moreover, scientific preparation and standardization will increase the cost of these indigenous drugs so that even that small advantage will be much minimized if not lost.]

Medicine is becoming an international science. In treatment chemotherapeutic agents and biological products, often synthetic, are sweeping the board. No country can ignore this fact and base its therapeutic on ancient vegetable remedies even if scientifically prepared and standardized. The people of India need the best drugs available and India should produce them herself. The solution of the problem of the cost of drugs in India lies with the chemical manufacturers and the administration. The price of many effective and modern drugs, whether produced in India or imported, bears little relation to the cost of production. If the chemical industry can produce effective drugs at a cheap price with only a reasonable margin of

profit, many of the difficulties mentioned by Sir Ram Nath would disappear.—EDITOR, *I.M.G.*]

Medical News

REPORT OF THE HEALTH SURVEY AND DEVELOPMENT COMMITTEE

THIS Committee which was appointed in October 1943 under the chairmanship of Sir Joseph Bhore has just issued its report in four volumes: (i) A survey of the state of the public health and of the existing health organization. (ii) Recommendations. (iii) Appendices. (iv) Summary. It covers a very wide field ranging from medical aid and welfare work in the remote village to promotion of research work of the highest type. In drawing up the report the Committee had the benefit of the presence and advice of several experts from Britain, the U.S.A., Australia and U.S.S.R. The essence of the scheme is the district health organization, and the idea is to develop it from a modest beginning into one which will provide as complete a health service as possible. The plan has therefore been drawn up in two parts, one a comprehensive programme for the somewhat distant future and the other a short-term scheme covering a ten-year period.

Administration

On the administrative side the Committee proposes Ministries of Health at the Centre and in the provinces and health administration in local areas, with a Central Statutory Board of Health. The Centre, with its larger resources in money and technical personnel, should help the provinces with grants-in-aid for the development of the health programme and with such technical assistance as may be required.

Councils of experts

The Committee considers that the Ministries of Health, central and provincial, should have the advice and guidance of technical experts in the planning and maintenance of the health services and, therefore, recommends the creation of standing Councils of Experts at the three levels of central, provincial and local area administrations. These councils will consist of representatives of the medical, dental, nursing and other professions. It also recommends the establishment in the provinces of Provincial Health Boards and Health Councils with composition and functions similar to those of the Central Board and Central Council.

The Ministry of Health, central or provincial, will be the ultimate authority responsible for all health services operating within its jurisdiction and should have power to lay down and enforce minimum standards of health administration for those services which are within the immediate control of other departments. The Committee points out that the Central Government should be responsible for the enforcement of all measures necessary to prevent inter-provincial spread of infectious diseases. Enforcement of standards regarding food and drugs in the inter-provincial commerce should also be the function of the Central Government. In certain exceptional circumstances the Central Government should have power to direct action in a province in the interests of the country as a whole but normally action should be taken after consultation with the proposed Central Board of Health.

Recruitment of services

It is proposed that the principal technical adviser to the Ministry of Health should be the Director-General of Health Services at the Centre and the Director of Health Services in a province, who should function in each case as the single administrative officer for the curative and preventive department of health.

There should be separate Central and Provincial Health Services. These services should normally be recruited in India but for a few posts in teaching and research institutions it may be necessary to recruit suitable persons from abroad on short-term contracts. One-third of the posts in the general health services should be filled on merit; in filling the remainder, consideration may be given to representatives of the different communities. A proportion of the posts in the provincial cadres should have the same salary and status as their counterparts in the central service to facilitate exchange of officers between the Centre and Provinces. There should be no reservation of posts under the Central or Provincial Councils for the civil branch of the Indian Medical Service.

Health administration in the local areas

The Committee envisages a comprehensive health service with recruitment, staff and conditions of service on similar lines throughout the province and continuous and effective supervision by the higher technical staff over the work of the health personnel even in remote villages. In local areas there will be a single health authority, to be called District Health Board, in place of the existing multiple health authorities, and its jurisdiction will extend to the district as a whole. But certain large municipalities such as Calcutta, Bombay, Madras and Karachi which are governed by their own Acts as well as other municipalities having populations of at least 200,000 each and which may be considered as being in a position to maintain an independent health service, may be excluded. All these large municipalities should develop and maintain their own health organizations on the lines suggested by the Committee.

Every municipality included in that area under the scheme should be required by statute to contribute to the District Health Board not less than 30 per cent of its income from all sources other than Government grants and every district board or panchayat should similarly contribute not less than 12½ per cent of its income. Such contributions and any grants sanctioned by the Provincial Governments will constitute the funds to be administered by the Board. While the Board will enjoy a large measure of autonomy, it is essential, says the Committee, that the Provincial Minister of Health should have the power of ensuring compliance by the Board with the general policy laid down by him.

The District Health Organization will be in the charge of an officer to be designated the officer in charge of health services, who will be the Secretary of District Health Board and the Chairman of the District Health Council. District Health Services should be provincialized, and the whole-time-salaried doctors should be prohibited private practice.

Long-term programme

As far as possible, the administration district should be chosen as the area for the development of the scheme. An arbitrary figure of 3 million as the population for a district has been chosen and this is referred to as the 3-million plan.

The District Health Organization will have as its smallest unit of administration the primary unit which will normally serve an area with a population of about 10,000 to 20,000. A number of such primary units (15 to 25) will together form a secondary unit, a varying number of the latter (about 3 to 5) will form the District Health Unit, the designation by which the District Health Organization will be known. At each of the headquarters of the district, the secondary, and the primary units will be established a health centre as the focal point from which the different types of health activity will be carried out into the territory covered by each unit. The district health centre will possess general and special hospitals with about 2,500 beds, and all the consultant and laboratory services on up-to-date lines; the secondary health centre will have hospital accommodation of 650 beds, while the primary health centre will have a 75-bed hospital. By the time

the long-term programme is completed, the hospital accommodation will have risen from the present figure of 0.24 bed per 1,000 of the population to 5.67 beds per 1,000.

The health organization is based mainly on a system of hospitals and health centres of varying sizes and of different technical efficiency. These institutions will play the dual part of providing medical relief and of taking an active part in the prevention campaign. Work in connection with maternity and child welfare, tuberculosis, leprosy, etc., will be carried into the homes of the people from the health centres, at which social workers are to be employed in an honorary capacity.

Eventually the plan for a district with a population of three millions will consist of 150 primary units, each providing preventive and curative medical attention for a population of 10,000 to 20,000. Each primary unit would ultimately have a staff of 6 doctors, half of them women, 26 nurses for hospital duties and for work in the homes of the people, 6 midwives and 18 others, including social workers, sanitary inspectors and various other personnel. Thirty primary units would be attached to a secondary unit which would provide institutional facilities of a high order. Finally, 5 secondary units would look to the district headquarters, where ultimately a hospital will be developed making available medical aid of the highest standard in every department of modern medicine. These developments would take about 40 years to materialize.

Social medicine

The Committee emphasizes that suitable housing, sanitary surroundings and safe drinking water supply are prerequisites of a healthy life, and points out that the improvement of nutritional standards, elimination of unemployment and provision of a living wage for all workers and improvement in agricultural and industrial production and in means of communication, particularly in the rural areas, are all facets of a single problem and call for urgent attention.

Short-term programme

Under the short-term programme, the plan will be less elaborate. It is suggested that in view of the insufficiency of funds and of trained personnel, each primary unit should cater, during the first ten years, for a population of 40,000 (as against 10,000 to 20,000 under the long-term programme) and have a dispensary, instead of a hospital, with two beds for maternity and two for emergency cases, but a 30-bed hospital may be established at the start to serve four primary units. The secondary health centre is to start with a 200-bed hospital to be raised, by the tenth year, to 500 beds and the establishment of the District Health Centre will be postponed till after this period. The staffing and equipment of the health centres at the headquarters of the primary and secondary units will be on a reduced scale. The existing number of hospital beds in British India is about 73,000 and with the proposed new provision, the accommodation will rise at the end of first 5 years to 183,000 and at the end of first ten years to 353,000 i.e. one bed for every 1,000 population. In the sparsely populated areas it will be advantageous to supplement the primary health centres with travelling dispensaries.

The Committee then proceeds to make suggestions to improve the nutrition of the people and lays emphasis on the need for health and physical education of the general population. Health services for mothers, children and industrial workers are dealt with in turn, and many recommendations are made to control the prevalence of malaria, tuberculosis, smallpox, cholera, plague, leprosy, venereal diseases, hookworm diseases, filariasis, guinea-worm disease, cancer and mental diseases and deficiency. Town and village planning, rural and urban housing, water supply, general sanitation and other matters concerning environmental hygiene all receive due attention in the report, and recommendations are also made to improve the collection of data for vital statistics, which is well known to be very defective in India.

Professional education

One of the first necessities is a substantial increase of trained personnel. For the ultimate requirements of the scheme the number of doctors will have to be increased about 5 times, nurses about 100 times, midwives about 20 times and dentists about 90 times. The doctor of the future will need to attend the public health duties as well as dispense medical aid in the curative side as part of his day-to-day work. The Committee suggests an output of 4,000 to 4,500 doctors a year as the target to be aimed at in the first ten years or roughly double the present output. They recommend that there should be one standard of medical training, that of the medical graduate, and that the training of licentiates should be discontinued within ten years. A reorganization of the medical curriculum and the establishment in every medical college of a department of preventive and social medicine are proposed. Economic barriers should not prevent suitable students from entering the medical profession and students willing to enter public services after graduation should be given a stipend of Rs. 1,000 a year. About a quarter to a third of admissions should be reserved for suitable women candidates, if available. The importance of research is stressed, and whole-time teachers should themselves engage in research and encourage any student showing aptitude in this direction. Post-graduate education should be devised for training consultants and specialists, and facilities for refresher courses should be developed to raise the standard of medical practice. Recommendations are also made for training dental personnel and to provide facilities for pharmaceutical education. The training of compounders will eventually be dispensed with.

The Committee makes some strong remarks on the deplorable conditions under which nurses and midwives have to work in this country and remarks that without a considerable increase in their number it is impossible to proceed with the health programme. At present there are some 7,000 registered nurses, but the number required for the short-term programme is approximately 80,000. The Committee has suggested among other things the provision of a stipend of Rs. 60 per month for pupil nurses.

Medical research

After reviewing the existing activities, the Committee recommends the formation of a central medical research organization which should formulate policy in regard to future development, stimulate and co-ordinate research activities, recruit research workers and create training centres for them. Other recommendations include provision for improved laboratory services in the provinces, development of research in special subjects such as malaria and nutrition, and the investigation of the social and environmental factors affecting health and disease. The manufacture of biological products such as cholera, plague, TAB vaccine, vaccine lymph and anti-rabic vaccine will continue to remain, as now, government responsibility.

All-India medical institute

Side by side with the rapid production of as large numbers as possible of all categories of health personnel the Committee considers it essential to establish an All-India Medical Institute in order to bring together, in one place, educational facilities of the highest order for the training of doctors and of the more important types of health workers. The institute will also train selected candidates from the provinces for helping to man with suitable staff, the new medical colleges which will be established. It must have a medical college of its own with teaching hospitals and laboratories as well as a college to provide the highest type of nursing education. Applicants from all parts of India will be eligible for admission.

Malaria

Malaria is by far the most important disease in India. An expansion of the Malaria Institute of India and

the establishment of the provincial malaria organizations and malaria control units is recommended.

Delhi province as demonstration area

The Central Government should attempt to demonstrate in Delhi Province the effects of implementing the proposals of the Committee, the purpose being to demonstrate to the country as a whole what can be achieved through co-ordinated effort to improve the health and general prosperity of the community.

Indigenous systems of medicine

The Committee suggests that it should be left to the provincial governments to decide what part, if any, should be played by the indigenous systems in the organization of public health and medical relief. They point out that public health or preventive medicine is not within the purview of the indigenous systems which also do not deal with such aspects of medicine as obstetrics, gynaecology, and advanced surgery. The scientific system of medicine, they consider, must be regarded as neither Eastern or Western but as a corpus of scientific knowledge and practice belonging to the whole world.

Drugs and medical requisites

The Committee states that the final responsibility should rest with the Government of India for seeing that the country's essential needs for drugs and medical requisites are met in such a manner as to make them available in adequate amount and of proper quality to all sections of the people. In regard to all such articles as are of essential nature the country should be made self-sufficient as far as possible.

The population problem

The growth of population will become an increasingly serious problem. The prospects of emigration helping to lessen the pressure of population are remote and uncontrolled growth of population will eventually outstrip the productive capacity of the country. The Committee considers that the only practical steps that can be taken are, firstly, measures to raise the standard of living, and secondly, the spreading of the knowledge of birth control as far as the limitations imposed by the peculiar circumstances of the country will permit. All the members of the Committee are agreed that, when child-bearing is likely to result in injury to mother or infant, there is every justification for the practice of contraception and that Government agencies should give instruction in birth control methods in such cases. Some members consider that the State should provide such facilities to persons desirous of family planning for economic reasons also, while others hold that State action will be justified only if there is substantial support from public opinion.

Financial problems

The Committee points out that at present provincial government expenditure on curative and preventive health measures constitutes a very small fraction of the total provincial expenditure varying from 2.5 to 7.3 per cent and they suggest that this percentage should be raised considerably. The present provincial expenditure ranges from 3.2 to 10.9 annas per head. The Committee estimates that their proposals will involve additional expenditure of Re. 1-3-0 per head in the first year and Rs. 2-13-0 in the last year of the ten-year programme.

[Note.—Forensic medicine does not appear to have been considered by the Committee.—Editor, I.M.G.]

POISONING DUE TO WHEAT ADULTERATED WITH CONTAMINATED WEED-SEED

In view of the fact that large quantities of wheat are being imported into India now from all parts of the

world, the following abstract of an article entitled 'An unusual form of epidemic food-poisoning with neurological symptoms' by Denis Brinton, F.R.C.P. (*Proc. Roy. Soc. Med.*, Vol. XXXIX, No. 4, February 1946, p. 173) will be of interest.

For thirteen months from October 1942 the population of Aden had been intermittently affected by epidemics of this food-poisoning. Perhaps 450 persons in all had suffered; and from the first the people had correctly blamed the Abyssinian wheat which had been shipped to Aden from the earliest harvest after the fall of the Italian East African territories. According to the sufferers, this Abyssinian wheat was not only of poor quality, but contained a poisonous weed-seed, called in the local Arabic *miscara*, literally to be translated as 'tipsy' which is a first-rate description of the effects it produces in man. *Miscara* is a common weed in every wheat field of the Aden peninsula also, and the greatest care had always been exercised by the farmers to remove the weed and its seeds from the wheat, at all stages from harvest to milling. In samples of Abyssinian wheat, the hilum of many of the *miscara* grains showed a black discoloration which under a hand lens presented a mouldy appearance. Several samples of newly-wharfed Ethiopian grain were collected and counted, and found to contain *miscara* seeds in quantities up to 10 per cent.

Reconstructing the clinical aspects of this food-poisoning by questioning both those who had suffered and the doctors who had had charge of them when ill, it was learnt that from one-quarter of an hour to two hours after taking food made of this grain, a man would become dizzy, and be smitten with headache, marked generalized tremors, lassitude, slurred speech, and a staggering gait. Sometimes, there had been vomiting and diarrhoea, and less commonly nausea and abdominal pain. Subsequent events seemed to vary directly with the amount of poison taken. If the subject had fed well, he paid for it by quickly subsiding into stupor or even a coma from which it might be impossible to rouse him for so long as ten hours; but, if he had taken only a little, his earliest symptoms would not noticeably increase and he might be fully recovered in three or four hours. There were no deaths, and within seventy-two hours even the most severely affected were well enough to resume their usual occupations.

Specimens of *miscara* sent to England for botanical and chemical analysis revealed it to be a weed called the flax-darnel (*Lolium temulentum*); and suggested that the poisonous element was in the mould to be seen on nearly every weed-seed, and was probably a pyridine base of incompletely established chemical composition, known as temuline.

Poisoning by *Lolium* is known in India. That the poisonous element is probably the mould connected with the weed-seed is a new suggestion.

ANY QUESTIONS?

UNDER this heading the editor will receive and answer questions of general professional interest, subject to the limitations mentioned in the last paragraph of the publishers' notice. The answers will be prepared by competent authorities. Anonymous communications will not be attended to. The name and address, however, will not be published, if so desired.

ANTIDOTE TO ARSENICALS

(Abstracted from the *Lancet*, ii, 29th December, 1945, p. 854)

EARLY in the war Professor Peters and Drs. Stocken and Thomson of the biochemistry department at Oxford set out to find an anti-arsenical substance and have now described the results of their research in the field of chemical warfare which led to the discovery of BAL (British anti-lewisite). This antidote should make the arsenical war gases obsolete, but it is also applicable to the treatment of the complications of arsenical

therapy such as dermatitis and encephalitis, and probably to some other metallic poisons as well. The discovery is based on the evidence that the high toxicity of trivalent arsenicals is due to their combination with two—SH groups in the pyruvate oxidase enzyme system to form stable arsenical ring compounds. It was thought that dithiol compounds by forming more stable ring compounds can release arsenic from the tissues.

BAL is an oily substance capable of penetrating the skin. When it is applied to tissues containing a trivalent arsenical compound, combined arsenic is transferred from the tissues to the BAL and is so excreted; thereby the toxic agent is removed. Treatment was at first applied by inunction which was later superseded in the U.S.A. by intramuscular method, using as a vehicle 10 per cent benzyl benzoate in arachis oil. The initial dosage now recommended is up to 4 mg. per kg. body weight at intervals of four hours. In a preliminary report to the Medical Research Council, half of the 30 cases treated were said to have responded favourably. If this success is maintained, BAL is certainly better than any other remedy so far described. It is, however, not free from toxicity, and until the stage of clinical trial is over, its use should be well-controlled. Kidney damage is not a contra-indication to its use, but it should be withheld in cases of liver damage.

SINGUR HEALTH UNIT

THE unit is situated in Bengal about 21 miles from Calcutta and is intended to provide the All-India Institute of Hygiene and Public Health with a controlled practice field for investigation and teaching public health.

Administratively a co-operative activity between the Government of India and Government of Bengal, the Health Unit is intended to demonstrate methods of public health administration in rural areas within the level of expenditure that the country can afford. It also affords opportunity for training medical and public health personnel, particularly the D.P.H. students of the Institute.

Three local groups—a Unit Public Health Advisory Committee, a Union Health Committee and Village Health Committee—are the channels through which the people themselves organize measures of public health in their villages. There is one village health committee for each village or Unit of approximately 200 families. Each village committee has five members elected by the villagers themselves and responsible for learning routine activities in connection with vital statistics, maintenance of tube wells, control of malaria and epidemics and maternity and child welfare.

This system enables the paid technical staff to undertake supervisory duties, execution being left to members of the village health committee serving generally as voluntary technical men except under special circumstances.

There are 42 primary and 10 schools of other categories in the Unit. So far 50 teachers have been trained in school health work, and through these teachers the school health programme of the Unit is pushed forward.

The public health administration section of the All-India Institute of Hygiene and Public Health at Calcutta is responsible for the over-all administration of the area. Other sections of the Institute cover a wide range of health activities like bacteriological analysis of water, investigation and control of communicable diseases, experimental feeding for nutritional and dietetic research, vaccination, physical examination of school children, care of pre-natal women and provision of satisfactory and cheap type of latrines.

The Health Unit, at present, has a population of 62,736 in 68 villages comprising an area of 33 square miles. Eventually it will consist of the Serampore Subdivision, Hooghly District, with a population of approximately 500,000.

Public Health Section

THE INFLUENCE OF FEEDING ON INFANT MORTALITY

By JEAN M. ORKNEY, M.B., D.P.H., W.M.S.

(From the Maternity and Child Welfare Clinic, All-India Institute of Hygiene and Public Health, Calcutta)

INFANT feeding is recognized as having a profound influence on the life and health of the infant. In the West, where, before the war, the decline of breast feeding was causing anxiety, many studies were made of the reasons for this failure at one vital phase of the reproductive cycle. In India, there is little statistical indication of the position regarding the establishment and maintenance of breast feeding. The following data collected during an analysis of record cards maintained for the field area covered by the staff and students of the Lady Reading Health School, Delhi, is therefore of interest not only as evidence of the high incidence of breast feeding but also as tentative support for the clinical experience of the danger to the child life associated with artificial feeding in the early months of life, and of the detrimental effects of prolonged breast feeding, without additional diet supplements, in the population group studied.

Material studied.—The cards analysed include 302 cards of infants dying during 1940, 1941 and 1942. The control group consists of 290 infants born during 1941 who were still in the area and alive at the end of one year. The total number of cards issued in 1941 was 505; of this number of infants, 290 survived to one year, 101 died and 105 left the area before completing one year, 9 were untraced.

The exact percentage of infants born in the area who were not contacted is not known, but it is unlikely to be more than 5.

During the 3 years covered by the survey, the area served remained unchanged, and 507, 505 and 557 infants were given cards. The increase in 1942 can in large measure be explained by the influx of mill and domestic factory workers into the area for war work, and by the increasing attention given to making cards for infants dying within a few days of birth.

Neonatal deaths numbered 26, 26 and 38 in 1940, 1941 and 1942.

The study was unfortunately interrupted by the transfer of the investigators concerned before the analysis of the cards of 1940 and 1942 survivors could be completed, and the figures presented are too small for sound statistical inferences.

The infant-mortality rates reported by the Medical Officer of Health, Delhi Municipality, were 175.7, 188.6 and 180.1 for the years 1940, 1941 and 1942. The infant-mortality rates for the centre area were 181.0, 221.7 and 190.3. These latter rates are calculated from the total number of infants given cards during the year

and the number of infant deaths during the year, no allowance being made for infants who left the district during the year. These figures, though not giving the true infant-mortality rate, are sufficient to indicate that the area is one of high infant mortality. The infant-mortality rates in the neighbouring city of New Delhi were 56, 68.4 and 52.2 for the corresponding three years. Geographical situation and climate can, therefore, have relatively little direct responsibility for the high rates in Delhi city.

Various factors influencing the high infant-mortality rate are being studied, but it is sufficient for the purposes of this note to say that the area is one of low economic status, consisting largely of small shopkeepers, hawkers, coolies, mill workers and families engaged in home industries and domestic factories, with a small sprinkling of middle-class families. Two hundred and ninety-five of the 592 families had an income of less than Rs. 5 per head per month (of these 64 families had less than Rs. 2 per head) while only 18 had a monthly income of over Rs. 20 per head. The environment is grossly insanitary and overcrowded, both from the point of view of density of population and houses per acre.

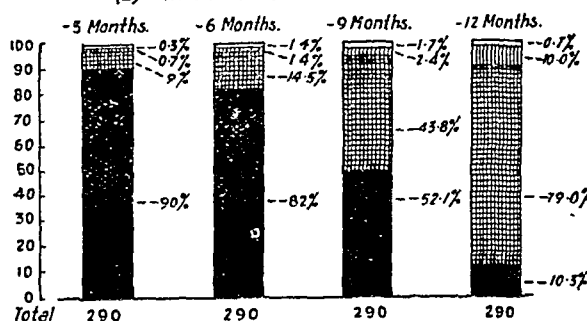
Incidence of breast feeding.—The percentage of infants, for whom breast feeding was established and maintained as shown in figure 1,

Fig. 1.

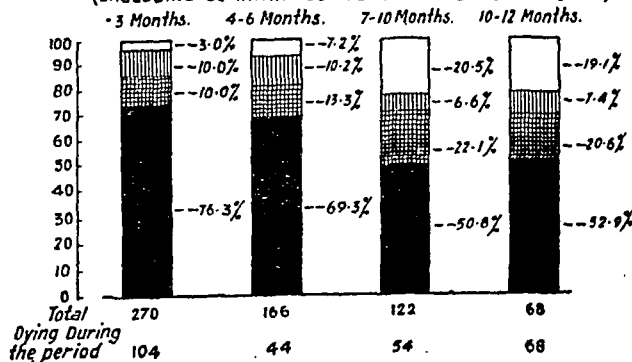
INFANT FEEDING AT VARIOUS AGES.

Wholly Breast Partly Breast Wholly artificial Unknown

(a) INFANTS LIVING ONE YEAR.



(b) INFANTS DYING UNDER ONE YEAR
(EXCLUDING 32 INFANT DEATHS WITHIN 48 HOURS OF BIRTH)



compares very favourably with the position in the United Kingdom, where rates published in the report on Infant Mortality in Scotland (Department of Health, 1943) vary from 32 per cent to 72 per cent at 3 months and 19 per cent to 58 per cent at 6 months. Deeny and Murdoch (1944) give a rate of 71 per cent wholly or partly breast fed at 6 months for infants surviving to one year in Belfast. Ghosh and Chandra Sekar found 95.8 per cent to 99.4 per cent of infants wholly or partly breast fed at one month in Calcutta (unpublished report).

From 0 to 6 months.—Combining the figures for complete and part breast feeding, 99.3 per cent of the survivors and 89.7 per cent of the dead infants for whom the information was available were breast fed up to 3 months, or to the age of death. At 6 months the percentage of breast-fed survivors was 98.6 and the percentage at the age of death under 6 months was 89.0 per cent.

The supplement added in the case of the partly breast fed was fresh milk in all but 2 cases where dried milk was used and one case where solids in the form of cereal had been introduced. The actual quantity of the supplement was not recorded, but from clinical experience the amount is known to be small. Few families in the area can afford to buy even 4 oz. or 8 oz. of milk daily and whatever is brought is shared by the entire family. Breast milk can safely be assumed to constitute the major part of the diet of the partly breast fed up to 6 months of age.

Artificial feeding consists mainly of fresh milk; dried, condensed and modified milk foods being too expensive.

From 7 to 12 months.—From 7 to 12 months complete breast feeding falls from 83.9 per cent at 6 months to 53 per cent at 9 months, and 10.4 per cent at 12 months amongst the survivors for whom the information was available. Amongst the deaths the drop is much less pronounced; 65.4 per cent of infants in this class were still wholly breast fed between 10 and 12 months of age. The figure is not comparable with that for survivors, since the latter represents feeding at 12 months, the former at 10, 11 or 12 months according to the age of death. A number in the mortality group are likely to have become partly breast fed had they survived to one year. The percentage of infants partly breast fed at 12 months is 79 among the survivors and 25.4 among the deaths for whom the information is available. Part breast feeding is the custom in the area and may continue up to three or four years of age if not interrupted by a subsequent pregnancy. No attempt has been made by the staff to discontinue the practice, because when the breast milk is stopped the child gets little or no milk at all and very little animal protein in any form.

Psychological difficulties do arise from the delayed weaning, but the real danger to life from the shortage of animal protein resulting

from weaning is judged to be more important than any potential danger to happiness.

The additions to breast feeding in the second half of the first year were fresh milk in 191 cases and dried milk in 5 cases. Solids, generally in the form of *suji*, were given to 56 infants between 7 to 9 months of age and to 190 infants of 10 to 12 months. Other less widely used cereals were *sago* and rice. Purées made from *dal*, from *sag*, carrot and other vegetables were generally taken at this age by only the small percentage of infants attending the centre regularly. No record of the quantity of solid food given to the infants was available from the records, but the difficulty of persuading the mother to give adequate quantities is well known to the medical and nursing staff of the Health School. Solid foods are not beyond the incomes of most of the families but the mothers find breast feeding easy and comfortable, and they are loth to give it up or to introduce new methods which involve extra time and trouble.

Reasons for artificial feeding.—Inadequate or spurious reasons for artificial feeding are not common in the area. Of the 29 infants artificially fed under 3 months, in only 3 could no cause be found apart from the mother's superstition that her milk would 'poison the child'. Eight of the 29 mothers were dead within 3 months of birth. In 16 instances the mother was either acutely or chronically ill, tuberculosis or severe anaemia being the most commonly noted disease. Cleft palate and breast abscess accounted for the remaining two cases of artificial feeding. In the 4 to 6 months group, death of the mother was the commonest cause of artificial feeding followed by severe maternal ill health. Six mothers died during the 4 to 6 months period making a total of 14 (6+8) maternal deaths within 6 months of delivery.

Breast feeding was maintained up to 3 months in all but 3 of the mothers who were physically capable of suckling their infants. There is thus no failure of the biological function of breast feeding in this group of low economic status in any case in which the pregnancy itself was desirable.

Influence of feeding on mortality

From 0 to 3 months.—The disastrous results associated with artificial feeding as practised in the area during the first 3 months of life are well brought out in figure 2. Of the group of 29 infants artificially fed during the first 3 months, 65 per cent died during the period, 93 per cent died at some time during the first year of life and only 6.9 per cent survived to one year of age. A considerable share of this excessive mortality must be attributed to the lack of vitality of infants born to mothers who were themselves seriously ill, to the exposure of the infant to massive tubercular infection and to less skilled attention from the mother or mother substitute.

Similar percentages for the wholly breast-fed group were 14.3 dead under 3 months, 55.9 surviving to one year. The partly breast-fed infants occupied, as might be expected, an intermediate position with 27.67 dead under 3 months and 47.2 per cent surviving to one year.

From 4 to 6 months.—During the 4 to 6 months period the artificially fed child still runs a very serious risk, 42.4 per cent dying during the period and 19 per cent surviving to one year. A larger percentage of partly breast fed than of breast fed died during this period and was 12.3 per cent against 5.3 per cent but the numbers in these two groups surviving at the end of the

Breast milk alone does not satisfy the nutritional needs of the child after 6 months in this area of low incomes and maternal undernourishment. The wholly breast-fed infant fails to gain weight satisfactorily, his nutrition and health progressively deteriorate, until finally he succumbs to infection generally of the respiratory or digestive tract. From 6 months onwards part breast feeding is the method of choice so far as the infant is concerned in an area where poverty precludes an adequate supply of fresh or processed milk, but the data in table I and figure 2 indicate that while breast

TABLE I
Nutrition of the infant at 6 and 12 months

	Good	Average	Under average	Poor	Unknown	Total
A. Survivors for one year.						
Nutrition at 6 months ..	171 (62.6%)	66 (24.2%)	29 (10.6%)	7 (2.6%)	17	290
" " " 12 " ..	42 (15.1%)	116 (41.7%)	90 (32.4%)	30 (10.8%)	12	290
B. Deaths before one year.						
Nutrition at time of death:						
— 6 months ..	83 (34.0%)	40 (16.4%)	46 (30.7%)	75 (30.7%)	26	270
— 12 " ..	12 (16.7%)	10 (13.9%)	28 (38.9%)	22 (30.6%)	50	122

year, namely 65.6 and 67.6 per cent respectively, are almost the same.

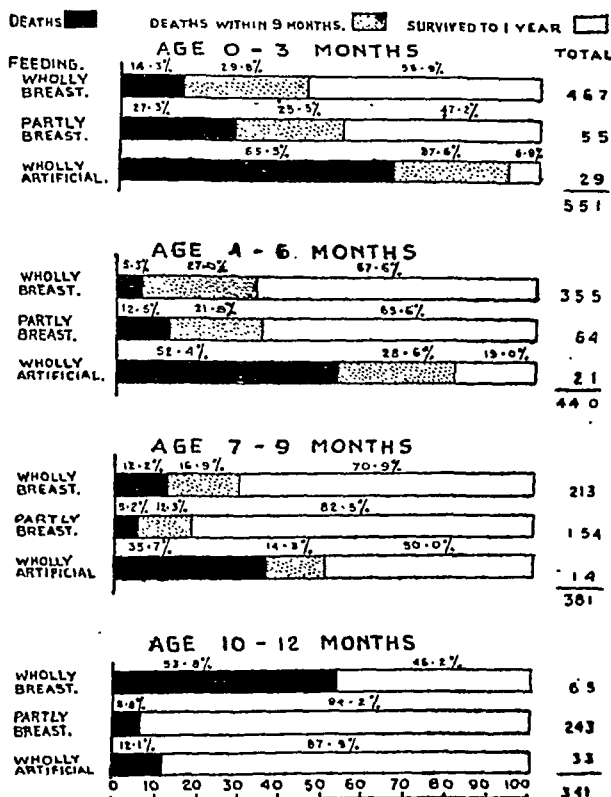
The gross adulteration and contamination of the milk supply in the area, and the primitive methods of preparing and administering the milk mixture to the infant might lead to the expectation that infection would expose the infant to a greater risk of death from gastro-enteritis. The similarity of the survival rates for the wholly and partly breast fed suggests, however, that the infection factor is not a serious one in the case of the partly breast fed. The explanation may lie in the fact that all milk is boiled after delivery to the home. The risk of recontamination from flies, filth and dirty utensils before the milk is consumed is undoubtedly considerable, but where milk is given in small quantity, as during the first 6 months, the milk is usually given soon after it is delivered, and spoon feeding is the usual method, a practice which is much less potentially dangerous than the brass 'lutia' with its long narrow spout and rubber nipple used for artificial feeding. The natural resistance of the infant who receives a fair supply of breast milk is also a factor of considerable importance. The higher incidence of deaths amongst the partly breast fed under 6 months is as much a reflection of inadequate total calories as of the bacteriological impurity of the cow's milk.

Wholly artificial feeding in this community is practically synonymous with gross underfeeding. The babies may survive for considerable periods growing progressively more and more marasmic until finally infection terminates the unequal struggle for life. Very few die immediately from acute gastro-enteritis.

From 7 to 12 months.—After 6 months the picture changes. In the third quarter the partly breast-fed children have the best chance of survival followed by the wholly breast fed; the mortality rate for the wholly artificially fed although lower than in the first 6 months is still very high. In the fourth quarter the percentages of deaths are 53.8 amongst the wholly breast fed, 12.1 amongst the artificially fed and 5.8 per cent amongst the partly breast fed.

Fig. 2.

EFFECT OF FEEDING ON INFANT MORTALITY



Note.—These percentages are useful only to compare the effect of differences in feeding practices and do not give the absolute risk to life in any group, as the data for infants with whom contact was lost are excluded, and the data includes deaths over a period of three years and survivors for a period of one year only.

feeding is well maintained it cannot be regarded as successful.

The number of infant deaths, instead of showing a progressive fall with age as in the West, rises from 44 in the second quarter to 54 in the third and 68 in the fourth quarter of the first year of life (figure 1), and table I shows the progressive deterioration of the nutrition of the infant between 6 and 12 months, which is again closely related to the quality and quantity of the diet.

The overall picture is one of undernourishment of both mothers and infants. An analysis of the relationship between the degree of care given by the staff of the Health School Centre and infant mortality shows that something can be accomplished by education and persuasion, but no considerable improvement can be expected until extra nourishment is provided for the expectant mother and the nursing mother within 6 months of birth, and for both mothers and infants from 6 months onwards. Foods alone, however, will not solve the problem; it is both uneconomic and unscientific to supply food without at the same time treating conditions which may prevent the full use of the food, such as

tuberculosis, chronic malaria and intestinal worms.

The influence of various factors on breast feeding

As might be expected in an area where breast feeding is practically universal except when physically impossible owing to the serious ill health or death of the mother, factors such as income, community (table II) and other factors studied, namely the attendant at childbirth, and housing, show no relationship which is statistically significant to the biological function of breast feeding from 0 to 3 months of age. Deeny and Murdoch (1944) also found that income, housing, domestic hygiene, order of birth and cause of death have no appreciable influence on the incidence of breast feeding in Belfast.

At 10 to 12 months the average income per head was Rs. 4.74 per month for the wholly breast fed, Rs. 7.89 per month for the wholly artificially fed, and Rs. 6.22 for the partly breast fed. The differences in figures are not statistically significant, though there is a vague tendency

TABLE II

Influence of various factors on breast feeding from 0 to 3 months of age

A. Income in rupees per head per month.			- 5	- 10	10 +			
Deaths	122	59	13			
Survivors	146	65	37			
Total in group	268	124	50			
PERCENTAGE OF WHOLLY AND PARTLY BREAST FED.			281	130	52			
			95.4	95.4	96.1			
B. Birth order			1	2	3	4	5	6
Deaths	36	35	32	22	27	24
Survivors	43	36	32	42	25	26
Total in group	79	71	64	64	52	50
PERCENTAGE OF WHOLLY AND PARTLY BREAST FED.			83	74	68	66	53	54
			95.2	95.9	94.1	96.9	98.1	92.6
C. Community			Mohammedan		Hindu			
Deaths	80		152			
Survivors	146		140			
Total in group	226		292			
PERCENTAGE OF WHOLLY AND PARTLY BREAST FED.			238		309			
			95.0		94.5			
D. Nutrition of nursing mother at 6 months.			Good	Average	Under average	Poor	Dead	
Deaths	21	101	85	15	6	
Survivors	9	154	99	15	..	
Total in group	30	255	184	30	6	
PERCENTAGE OF WHOLLY AND PARTLY BREAST FED.			31	257	190	41	14	
			96.8	99.2	96.8	79.2	42.8	

for prolonged breast feeding to be associated with the lower income levels.

Birth order.—The slight decrease of breast feeding for births of the order of 6 and over is statistically significant, a finding not unexpected in view of the known risk to the life and health of the mother associated with births of the higher order. The large proportion of births of the higher orders in this study is noteworthy. 7.8 per cent of the births shown in table II were ninth or tenth births and 4.4 per cent were eleventh or subsequent births. Burns (1942) found corresponding figures of 3.3 per cent and 2.1 per cent in a study of 16,500 pregnancies in Durham.

Nutrition of the mother.—There is a significant relationship between the nutrition of the mother and breast feeding when nutrition has been seriously impaired (table II) and this is in turn related to the economic status as shown in table III.

substantial reduction in the infant mortality rates in this area of low economic status can be expected.

Summary

Data concerning infant feeding obtained in a study of 302 infant deaths and a group of 290 infants surviving to one year in an area of Delhi city are presented.

Artificial feeding under 6 months of age and exclusively breast feeding after 9 months of age are associated with high mortality rates in the community studied.

Amongst the partly breast fed, underfeeding with consequent lack of resistance to any infection appears to be a more serious risk than direct infection from contaminated milk in the area.

Mortality rates in the 10 to 12 months age group are less amongst partly breast-fed infants than amongst infants who are wholly breast fed or who have been completely weaned, though

TABLE III

Nutrition of the mother at 6 months according to income for 567 cases in which the information was available

Income in rupees per head per month	Total	— 5	Percentage under Rs. 5 per month	— 10	10 +
Nutrition of mother—					
Good and average ..	310	163	52.5	105	42
Subnormal ..	196	119	60.0	52	25
Poor ..	51	41	80.0	9	1
Dead ..	10	6	60.0	4	0
TOTAL ..	567	329	..	170	67

Discussion.—The problem of feeding infants during the age period 6 to 18 months in a community of low economic status would be greatly simplified if proof were forthcoming that the addition of the relatively cheaper solids to the diet of breast milk resulted in well-developed children without causing undue strain on the mother. A detailed study of feeding during these ages seems to be indicated by the findings of this analysis.

While the extent of establishment and continuance of breast feeding at the various age levels is highly satisfactory, the results of breast feeding cannot be regarded as successful. The nutritional value of the diet supplied is already insufficient before the infant is 6 months old and it becomes seriously defective by the ninth or tenth month.

The health-visitor service can do something by education and persuasion to effect the introduction of solids into the dietary of the infant over 6 months, but until the nutrition and health of the mother is raised by various measures including the relatively easy provision of extra nourishment for the expectant and nursing mothers, and for the infants over 6 months of age, and by improved treatment of disease, no

in the latter case the difference is not significant

Income, housing, attendance at childbirth and religion within the limits of the community studied have no influence on the incidence of breast feeding. Birth orders of 6 and over are shown to have a slightly adverse effect, and there is a definite relationship between the incidence of breast feeding and the nutrition of the mother.

To Dr. Daisy Pereira, without whose help the transfer of data from record cards to schedules could not have been made, and to Mr. Chandra Sekar for valuable help with statistics my thanks are due.

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THE NURSING SCHOOL AND PUBLIC HEALTH NURSING*

By JANET D. CORWIN

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I AM very much honoured by the invitation of the Delhi Maternity Service Co-ordinating Committee to give its fifth annual lecture.

I feel particularly humble when I realize that previous lecturers have included such illustrious individuals as General Jolly, Colonel Lazarus and Dr. Balfour, especially in view of my short experience in India. However, quite apart from that, I feel it is of more than passing significance that you have chosen a *nurse* as your speaker this year. Therefore, I shall take this opportunity to thank you for this honour on behalf of the nursing profession in India, and also to congratulate you as a group which realizes that the nursing profession can be helpful in furthering your aims.

In her letter asking me to be your speaker Dr. Pandit says: 'The Delhi Maternity Service Co-ordinating Committee was originally organized to bring medical and public health services in the field of maternity and child welfare closer.'

This is a subject of which I am very fond. Co-ordination—joint activity—is one of the solid foundation stones of good medical practice in both curative and public health fields. This is true not only in maternity and child welfare services, but in the whole field of health. We are gradually learning that health promotion, disease prevention, and the cure of disease cannot be put into separate compartments, but must be thought of together as parts of a smoothly co-ordinated whole, each part as essential but supplementing and strengthening the other two. It is on this basis that I have selected my subject 'The Nursing School and Public Health Nursing' for to-night. Many of us think of nursing schools as associated entirely with curative work, and of public health nursing or health visiting as important only in the public health field agencies. My aim this evening is to show the need for these two fields to be drawn closer together in nursing, and to show something of how this may be done in an undergraduate nursing course.

Nursing is a very old occupation. It has existed as long as people have lived in social groups. The basic definition of 'to nurse' is 'to care for' and probably the first cave men called in a neighbour from a nearby cave to help 'care for' others in time of need. However, just as our modern concept of social living is more complete than that of the cave man, so our modern concept of nursing has broadened. 'Nursing' now means 'health conservation in

its widest sense, including the care of normal children and adults; the nursing or nurture of mind and spirit as well as body; health education as well as ministration to the sick; the care of the person's environment, social as well as physical; and health service to families and communities as well as to individuals' (National League of Nursing Education, 1937). It is in this sense that I shall speak of it to-night.

Nursing is closely related to medical practice. Each supplements and complements the other. Nursing could not exist without medical practice and thoughtful doctors in every country realize that *good* medical practice, whether in hospital or public health field, cannot exist without *good* nursing service.

Nursing is a service for the good of the people in a community. Therefore, it must be planned to meet the health problems of the particular people it serves. Since we are all most concerned with nursing in India, what, then, are the health problems of India?

Vital statistics give us a good indication of some of these.

Grant (1943) gives the following statistics for India in 1937:

Death rate = 22.4 per 1,000 population
(12.4 England and Wales).

Birth rate = 34.5 per 1,000 population
(14.9 England and Wales).

Even more startling figures are those for the city of Calcutta in 1940, where the death rate (27.6) was higher than the birth rate (26.1) (Hutchings *et al.*, 1944).

Infant mortality, a fairly good index of general health, was 162/1,000 live births. That is to say, approximately 3 infants in every 20 never even lived to reach their first birthday. Many of these deaths are preventable, as this group knows very well.

Let us see what other specific causes of death are. In India, in 1939, there were just over 6 million deaths (Nursing Information Bureau of the American Nurses' Association, 1943). Twenty-three per cent were due to malaria, that is, almost $\frac{1}{4}$ of the total deaths. Dysenteries and diarrhoeas accounted for over 4 per cent and cholera and smallpox for over 2 per cent. These are all preventable diseases. Though these statistics are probably not entirely accurate, they do give some indication of actual conditions.

Other health problems include widespread malnutrition, ignorance and superstition, the large proportion of acutely ill in all hospitals, and the recurrence of disease. I am sure all of you can recall many illustrations of these problems.

These, then, are some of the important health problems in India. What type of worker must we prepare to meet the nursing needs of the community?

In the first place, because of so much acute illness, she must be a good bedside nurse. This is something upon which many of us have been

* Being an address delivered at the Fifth Annual Lecture at the Delhi Maternity Service Co-ordinating Committee.

concentrating for many years. I want to stress a few special points this evening. Modern medical treatment is undergoing many changes to keep pace with new discoveries. The development of treatment by the sulpha drugs and penicillin, the perfecting of new techniques in bone surgery and the standardization of new immunological products, are a few of the important ones. Because of the nature of these developments a strong background in sciences such as anatomy and physiology, chemistry, physics and bacteriology is essential to good bedside nursing. Sciences can be taught adequately only through actual laboratory work. A good bedside nurse must also understand the techniques of nursing care, and must be able to carry them out accurately and skilfully. This ability comes not only from study in the library and class-room practice, but from constant educational supervision in the class-room and in the wards throughout the three years of training.

In the second place, to meet India's nursing problems our worker must have a knowledge of health, both physical and mental. Unless she has an understanding of the functioning of the normal, healthy body, she has not an adequate basis for teaching health nor for understanding deviations from the normal in disease conditions. For this, study of psychology and mental hygiene, and of sciences including nutrition, is important.

A third essential is a sound knowledge of disease and—an important part—of disease prevention. We have seen how many deaths occur in India from preventable causes. It has been emphasized increasingly in recent years that the prevention of disease is the most logical and economical basis for medical work. And what could be more sensible than to try to prevent disease entirely if possible—or if not that, then to prevent serious and prolonged illness by early diagnosis and treatment—or if not that, then to prevent recurrence of disease by education and by rehabilitation?

Health promotion, disease prevention, and the cure of disease cannot be put into separate compartments in nursing any more than they can in medical practice. Knowledge of public health nursing techniques is important in hospital just as knowledge of curative techniques is important in field work.

In connection with the prevention of disease, I should like to mention a few special types of knowledge which the nurse must have. Again, sciences are basic, and this time I would like to put particular stress on bacteriology. Unless the nurse is thoroughly convinced that certain diseases are caused by micro-organisms, unless she understands how infection occurs and how immunity is developed, she cannot possibly convince herself of the need for carrying out strict medical and surgical aseptic technique, nor can she convince others of the presence of these organisms which cannot be seen.

Another special type of knowledge which the nurse needs is an understanding of the relation of social and economic factors to health. The need for this in India is particularly great. Still another is knowledge of how to teach. Health teaching is an increasingly important function of the nurse. Too often in the past we have considered that if someone had a sound body of knowledge himself he unquestionably could teach it to others. We realize now that the ability to impart knowledge does not necessarily accompany the ability to absorb knowledge. Study of methods of education makes teaching more effective and learning quicker and more complete.

I shall speak of only one more characteristic which a worker needs to meet the nursing problems in India. Earlier this evening I mentioned the interrelationship of good medical practice and good nursing. In order to fulfil the demands which are, and should be, made upon her in such a relationship, the nurse must be able to offer more than instinctive obedience. She must have the ability to give intelligent co-operation. The basis of this capacity is a greater emphasis in her preparation upon *principles* and less on repetitive training, more attention to self-discipline and to individual thinking. These help to develop a person capable of meeting the needs of the many sided branches of modern nursing in which the nurse is not constantly under direct orders but must frequently take action on her own initiative. Particularly in community nursing must she be competent to act independently, since the doctor is not always close at hand.

So far I have been speaking almost entirely in terms of nurses and nursing. I shall diverge for a moment now to discuss the position of the health visitor. A health visitor's training is based upon a midwifery course with an additional 12 to 18 months' training in which theory and practice, to all intents and purposes, are limited to maternity and child welfare. We have seen in our brief review of the health problems of India, that many problems in the public health field lie outside the field of maternity and child welfare. In fact, already India has found it necessary to try to prepare other specialized workers for other specialized fields, such as those related to tuberculosis and venereal disease.

In all other countries where modern public health organization and methods are in practice, a person whose fundamental preparation is in nursing, that is a public health nurse, has been the basic worker in the public health field. Also, it has been proved that it is both more effective and more economical to have one worker capable of carrying out a generalized programme rather than many specialized workers. By a generalized worker is meant one who can carry on many different types of activity such as communicable disease control, school and industrial hygiene, and maternity and child welfare, rather than just one, such as maternity

and child welfare. My own conviction is that, although health visitors have done a useful job and will be needed for many years, public health programmes will be seriously curtailed until public health nursing is established in India. In talks with medical and nursing leaders in the past 8 months I have found others as firmly convinced of this as myself.

Now we have seen what some of India's health problems are, and the type of worker necessary to meet nursing needs arising because of these problems. Is this worker being supplied? Let us examine the present situation in India. All of you who are present here this evening are familiar to some extent with present conditions. Some know a great deal more than I do. My own knowledge is based upon two sources of information. One is personal observation in many parts of India, which has been fairly widespread though unfortunately it covers a period of only 8 months. The other, and one which has been of the utmost value, is having the opportunity to talk to medical and nursing leaders whose experience in India is broad and who have been working to improve the present situation for many years.

Firstly, what types of worker are there? We have nurses, who are trained for work in hospital. We have health visitors. We have midwives. And we have a growing number of workers prepared in very short courses to meet particular problems in one field, such as tuberculosis or venereal disease, school health or industrial hygiene. There are great variations in educational and cultural background among all these workers.

How many workers are there? There are about 7,000 nurses, about 800 health visitors, and about 5,000 registered midwives for India's 400,000,000 population (Hutchings *et al.*, 1944). This gives us a figure of at most 13,000 and a ratio of about 1:31,000 population. Compare this with the ratio of nurses to population in England and Wales, 1:465 (1937); and the U.S., 1:357 (1940). Compare also the ratio of nurses to practising doctors in the three countries:—

England—2 nurses to 1 doctor.

U.S.A.—1½ nurses to 1 doctor (Statesman's Year Book, 1944).

India—less than ½ nurse, health visitor or midwife to 1 doctor.

The figures point out the inadequacy of the present supply of workers.

The training schools provide our supply of workers. Therefore, most of my comments now will be in relation to these schools.

What type of preparation do our workers have? This varies from the 3-year nursing course down to short courses of a few months for some of the special workers. In all courses one fact stands out which conditions the preparation of all workers. Education is subordinated to the service demands of the institution which is providing the training. Pupils are considered

much less as students than as service personnel. This fact cannot help but limit the type of curriculum which is planned, and usually the time spent on theoretical teaching is small as compared to the time spent on practice. Also, practice is planned, not according to the educational need, but according to service demands of the hospital or other agency. These results are inevitable under present conditions. The demands of nursing service exert unrelenting pressure. A solution is the establishment of schools independent of service demands, in which the students' time can be controlled by the school and used as seems best from the point of view of the students' learning. There is no such school in India to-day.

In many schools science courses are very limited. Chemistry, physics, and bacteriology lessons are seldom given, and laboratory work, if given at all, usually consists only of demonstrations. It is in the sciences which the worker finds many of the principles upon which her work is based. This is true in both hospital and public health nursing.

Principles must be backed up by the knowledge of how to put the principles into practice in relation to both health and disease conditions. I should like to speak of two things which are important in this connection. One is the specific knowledge gained from courses such as medicine or surgery, medical nursing and surgical nursing. I think we all realize the need for including this type of course in the curriculum. The other is help in putting knowledge into practice, by means of supervision and teaching in class-room and in the ward or the public health field. Therefore, we must think of the amount and kind of teaching staff provided.

In present schools of nursing, we sometimes find one member of the nursing staff, the sister-tutor, who has the full-time responsibility of teaching students. (Sometimes we find that there is not even one full-time teacher and that several other sisters must share the responsibility for teaching.) One person cannot give adequate teaching and supervision to all students of three different years. Even if the ward sisters are expected to take some of the responsibility for teaching and supervision in the wards, they are often so overburdened with administrative duties and with the struggle to get patients nursed that they have neither time nor energy for extra duties, and teaching slips into the background. These conditions mean that the students do not have enough help in learning the fine points of good nursing care and that they may even endanger their patients—not at all intentionally, but because they have not had enough help in learning. Also, it takes students longer to learn because their learning is not directed.

Another difficulty is that most of the sister-tutors have not had special education in teaching

nursing. Formerly, this training was not available in India, but now the School of Nursing Administration in Delhi offers a course to prepare sister-tutors as well as nurse administrators, and it is meeting a real need. However, it is hampered in its work by having to fill in gaps in knowledge which should have been part of basic nursing courses. It cannot plan all its work on a truly graduate level.

We have seen the lack of adequate science background in the present schools, and the lack of adequate teaching and supervision. Unless the worker has a sounder basic training she cannot take, or be given, as much responsibility as modern nursing demands. She cannot think for herself beyond a certain point. She can offer obedience but not intelligent co-operation, which makes nursing care most helpful to the doctor and which relieves the doctor of many small responsibilities which he has to take now but of which he should be relieved.

There is another large and important body of knowledge for which there is no provision in the curricula of present schools of nursing. That is the knowledge relating to the public health aspects of nursing. I have told you of my conviction that, even in hospital work, there is great need for nurses to have knowledge of health and of prevention of disease. I mention it here but shall wait until later to discuss it in relation to the nursing school.

Closely related to the curriculum of the school are the opportunities available to students for practice. We all know that one cannot learn to be a nurse without practising under good conditions where good nursing is being done. At present, the entire practice field of schools of nursing is the hospital ward. There are two characteristics of this practice field which I should like to mention to-night. One is that hospital wards to-day are admittedly overcrowded and understaffed. From the point of view of the need of hospital beds by sick people, this is probably inevitable, and patients are getting far better care than they would if they were not in hospital. We all admire the devotion of nurses in these busy hospitals. However, from the point of view of *the education of the student*, the overcrowded, understaffed wards are unsound. Not only does the student nurse see hasty and sometimes poor nursing care carried on by other nurses, but she must do the same thing herself to get through her work.

The second point in relation to the hospital practice field is that the students' practice is often limited to those services available in the hospital to which her school is connected. In a large general hospital for men and women a wide variety of services may be found. However, in other schools, students get a limited practical experience. In some cases they have no opportunity to nurse male patients. Sometimes the children's wards are too small. Almost always there is no practice in nursing either

communicable diseases such as tuberculosis or in nursing patients with mental disease. All of these are considered essential in modern schools of nursing in many countries.

Now, a word about the public health field agencies which are not being used for nursing students at present. The main interest of health visitors has been maternity and child welfare, and there are a few rather limited practice fields for this specialized work. However, fields for practical experience in other types of public health work are practically non-existent. Another part of the practice field for public health nursing in other countries is found in the out-patient clinics of hospitals. Though under present conditions student nurses in India may be sent to work in the out-patient clinics, it is not with the aim of giving them practice in public health nursing techniques such as health teaching. Out-patient clinics at present have little value as public health fields, since emphasis is on curative medicine rather than on the prevention of disease and the promotion of health.

Our next question in relation to the present situation in schools concerns living and working conditions. These are beginning to receive the attention they deserve, so I shall only pause to say that every effort should be made to bring them to a good level. Sleeping quarters have been crowded, unattractive, and unhygienic. Dietary standards and the protection of health have been inadequate. Hours of work have been long and arduous. Stipends have been small and on the basis of wages for service rather than of scholarships for students. Libraries, one of the essential teaching aids of modern education, have been very limited. Proper recreational activities have been meagre. We cannot call our school of nursing professional schools, unless they offer conditions on a professional students' level. We cannot attract enough students of the calibre we want unless we offer suitable conditions of living and working.

What then can we conclude about whether or not the type of worker we need to meet the nursing needs of India is being supplied? Is the present state of affairs satisfactory? I think everyone will agree that the answer is no. Then what is to be done?

Can we start to-morrow and make a complete change? Shall we discard all the people who have been working for many years but who are not as well prepared as they should be to meet India's health needs? Again, no, of course not. We need all of them. For one thing, India has 400,000,000 population and tremendous nursing needs which we have hardly begun to meet. There is not only room for, but a crying need for all the present type of workers, and there will be for many years to come. For another thing, the number of women in India who have graduated from secondary school and university is woefully small. Unless and until this number

is increased, preparation of workers on a more complete basis cannot be sufficient to meet India's needs, and they must be supplemented by other workers with less training. Again, preparation based on educational needs of the student rather than on service demands of an institution is more expensive. Health and medical services would find the cost of such education for all workers more than they could bear. And, finally, good preparation cannot be given without qualified teaching staff in sufficient numbers, and without practice fields on a high level both in hospital and public health fields. At present there are neither sufficient trained staff nor sufficient practice fields of this type available to meet the need of all schools of nursing.

Then what can we do? It seems to me that we have two particular needs on which we should concentrate first, because by meeting these needs we will help to meet all other needs.

In the first place, we need nurses who are prepared to do public health nursing, both in the hospital and in the public health field agencies. Without nurses with this knowledge, there are large gaps in a complete medical and health programme for India.

In the second place, we need more nurses who are capable of teaching and supervising in both hospital and public health nursing. Without more teachers we cannot hope to meet the demand for the large numbers of nurses India needs. Without more supervisors, it is unfair and sometimes even dangerous to put demands upon other workers who have had the opportunity for only incomplete training. Supervisors and teachers are both needed in order to improve standards of work.

Preparation for both these activities can begin most successfully with the undergraduate nursing course. From the point of view of public health we have seen the trend toward co-ordination of activities for the promotion of health and the prevention and cure of disease. Just as these cannot be pigeonholed and separated in practice, neither should they be in nursing education. In a course combining preparation for all three activities, valuable time and money are saved and a better worker results.

From the point of view of teaching and supervision, all people carrying on these functions need a solid foundation of knowledge and high standards of practice. We certainly do not expect nurses to fill teaching and supervisory positions immediately after their undergraduate course. Experience as a graduate nurse is indispensable in the preparation of higher personnel just as knowledge and high standards of work are needed. However, we again waste valuable time and money unless we start sound, complete preparation at the earliest possible moment. That moment is the beginning of the undergraduate nursing course.

Therefore, what is our fundamental and essential need right now to help us to meet

more adequately the nursing problems in India? It is for a school of nursing of high calibre—one model undergraduate school to start with—which will give a combined preparation for both curative and public health nursing.

In the short time remaining, let us review briefly some of the characteristics such a school must have.

The school must be independent of demands for service by hospital or any other agency. Only when this is true can the practical experience of the students be planned according to their needs as students. The budget must be large enough to provide teaching staff, living and working conditions, equipment and library facilities which will allow the school to carry out its educational plans. Probably it should also provide some stipends for students. These must be on the basis of scholarships rather than wages for service.

To achieve financial independence, funds must be obtained. These may come from various sources, such as subsidy by central or provincial governments or by university, from endowments, gifts, and student fees, or from a combination of these.

Control of the school may vary according to the source of its funds. For instance, it may be directly under government control or it may be under a university. In any case, the executive control must be given by the governing agency to a nurse director who is an expert in nursing education. She should have a committee composed of representatives from such groups as doctors, nurses, and educators to advise her, but the nurse-director should direct the school.

The choice of students must be given careful attention, since without students of good calibre there is no use in planning curriculum and teaching on a high educational level. Selection of students should be made by a group, drawn from the faculty of the school, who understand what the school is trying to achieve. Students should have at least passed from secondary schools and with higher education if possible. Cultural as well as educational background is essential. Three important characteristics which each student must have are intelligence, health, both physical and emotional, and real interest in nursing. This last, as we know, is particularly difficult to determine before admission.

The faculty of the school must be carefully selected, as it is the type of teaching and supervision which is done that determines whether or not the educational purposes of the school are fulfilled. Nursing staff must be highly qualified not only in their own fields of nursing but in teaching methods, and they must be the kind of people that we wish our students to emulate. The number of nursing staff is also important. Number depends upon the number of students in the school and the type of course given. Medical and other teaching members of the staff must be qualified as teachers in their own

fields and must also understand the particular needs of nursing.

Practice fields in both hospital and public health departments must be adequately staffed so that a really high standard of nursing care is possible. As graduate nurses we may have to modify standards in certain situations, but as students we learn what high standards are. Unless we do, we will never be able to practise them even under ideal conditions.

Practice fields must be extensive enough to give the student opportunity to work with a wide variety of people both in health and disease.

Living and working conditions must be suitable to professional students and to the staff of a professional school. Some of the factors which must be considered are residence accommodation and living amenities, health protection including the nutritional standard of the meals provided, hours of work and study, opportunities for healthful recreation and for personal growth, and the general emotional atmosphere.

The basis of the work of the school is the curriculum. We have time this evening to point out only six of the most important principles which must underlie it.

In the *first* place, it must be based upon a definite philosophy of education which must pervade the whole work of the school. *Secondly*, it must be planned to meet the specific nursing needs of India. Earlier this evening we discussed some of these needs. Because of them we must include in the curriculum a number of science courses including laboratory work. These should include anatomy and physiology, physics, chemistry, bacteriology, pathology, psychology and nutrition.

We must also include a study of so-called public health aspects of nursing. This means that the normal individual as well as the abnormal will be studied, and that the normal will be studied first. Prevention of disease as well as the treatment of disease will be emphasized. Social and economic factors in relation to health will be studied, and the community and family from which people come and to which they return will be given attention. We will teach the students how to teach health and we will help them understand the important place which nurses should take in the teaching of health. We will give students public health experience through observations and through practice in out-patient clinics and in the public health agencies and we will count on not just one but on every single member of the school of nursing faculty, both doctors and nurses, to point out public health aspects of his or her own particular field.

We must also include in the curriculum sound preparation for bedside nursing, through practical classes in nursing in the school, through supervised practice in the wards, and through ward teaching programmes.

We must include study of the various branches of medicine, such as medicine, surgery, paediatrics, obstetrics and communicable diseases, and the specialized nursing in each field.

We must include courses which give the student an understanding of the past and future of nursing and of her particular responsibilities as a member of the nursing profession.

A *third* principle upon which the curriculum should be based is that theory and practice must be correlated throughout. For instance, when a student is having practice in the surgical wards she will have classes in surgery and surgical nursing at the same time.

Fourthly, time allotted to classes, study and practical work will be that suited to the status of student. She will have more time for classes and for study than at present.

Fifthly, students will be given time to learn but repetition of thoroughly learned activities will be avoided. This is perhaps particularly important in relation to practical work.

Sixthly, methods of teaching and supervision will be chosen to help the student to think and to become a responsible person.

This is far from a complete picture of the school. However, I have tried to indicate a few of the most important characteristics.

To-night we have discussed some of the health problems of India, which Indian nursing as a service for the Indian community must help to meet. We have seen what characteristics a nurse should have to meet these problems. We have seen that present types of workers are not adequately prepared for the task, and we have discussed the need for a model undergraduate school of nursing, preparing for hospital and public health nursing, as the basic need in improving the present situation.

In conclusion, I should like to tell you of the remark of a nurse which I heard sometime ago. 'You know', she said, 'the sulpha drugs are killing nursing'. I think that she meant to say 'The sulpha drugs are *changing* nursing'. The sulpha drugs symbolize the tremendous advances which are taking place in medicine and in the whole world to-day. Medicine is changing because of these new discoveries. Nursing and preparation for nursing must also change. They have no choice, for no one can ever stand still. Unless we progress, we go backward, because the world is progressing all around us. It will not wait for us. Therefore, let us not be content with the present conditions in nursing in India. Let us begin now to prepare nurses who can help to a greater extent to meet India's nursing needs. Let us all work to develop that model school of nursing.

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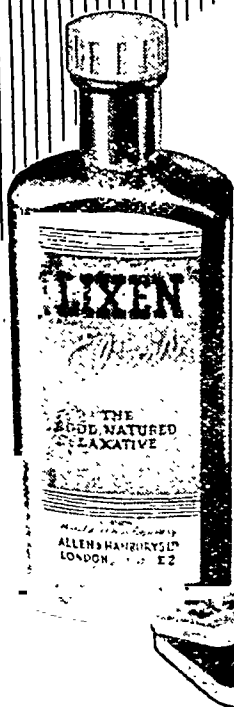
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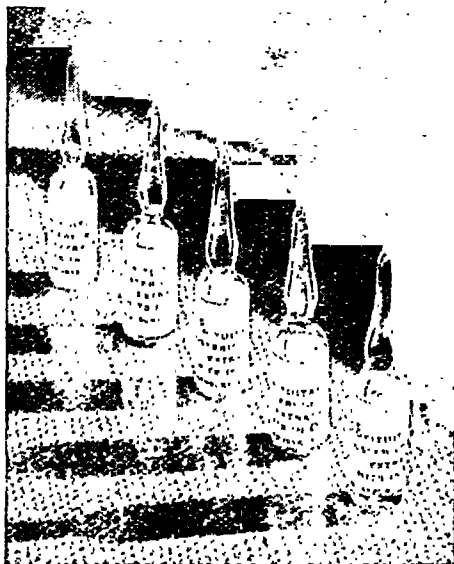
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ERRATUM

In the *I.M.G.*, 80, 12, p. 633.

The Wassermann positive rate of cases from hospitals and venereal clinics of Calcutta in 1939, 1943, 1944 and 1945. By S. D. S. Greval, A. B. Roy Chowdhury and B. C. Das.

In column 2, para 2, line 2, for 'below' read 'before'.

Current Topics

The Serological Diagnosis of Relapsing Fever

By G. J. STEIN

(Abstracted from the *Journal of Experimental Medicine*, Vol. LXXIX, January 1944, p. 115)

1. SPIROCHÆTES of relapsing fever have been separated from the blood of heavily infected mice and rats by hæmolysing with saponin, followed by repeated washing of the spirochætal suspension with physiological saline.

2. Spirochætes obtained in this manner appear to have broad antigenic specificity. Antigens of this type fixed complement in the presence of serum obtained from man or animals infected with one or other of the recognized strains or 'species' of relapsing fever spirochætes. Macroscopic agglutination of the antigens likewise was observed with sera from the same sources.

3. Positive serological reactions were not observed with convalescent sera obtained following infection with other diseases, for example, typhus fever, malaria, Rocky Mountain spotted fever, Weil's disease, syphilis, and typhoid fever. Hyperimmune sera prepared against other pathogens also failed to react with the relapsing fever antigens.

4. No apparent change in the antigen occurred following storage in the ice box for as long as 4 months.

5. The results indicate that treatment of the spirochætes of relapsing fever with saponin yields a relatively stable antigenic preparation which may prove useful in the serological diagnosis of this disease.

On the Employment of Quinacrine Hydrochloride in the Prevention of Malaria Infections

By M. F. BOYD

and

S. F. KITCHEN

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXV, July 1945, p. 307)

From the data submitted it appears that *P. vivax* and *P. falciparum* react differently when inoculated into white patients routinely receiving quinacrine. The observations of experiment C indicate that the administration of 0.1 gramme six days a week continued during the period of exposure has afforded complete protection against the acquirement of a falciparum infection, but has not protected against a vivax infection. Even the materially lower dosages in the continued regimens employed in experiments A and B appear in some

instances to have protected against the acquirement of falciparum infection, and in the instances when the infection became patent, appear to have exerted a therapeutic effect before the onset of clinical activity.

The observations of experiment D indicate that when the period of administration closely coincides with the time of exposure, doses of 0.1 gramme per day for six days a week are inadequate to protect against the acquirement of a vivax infection.

Even when the period over which these doses are given is extended to at least two weeks before and two weeks subsequent to the time of exposure, vivax infections later become clinically active, although exhibiting a more extended incubation period. Since it is well known that vivax infections may, even without suppressive therapy, sometimes present protracted incubation periods approaching a year in duration, it is likely that a high proportion of individuals who have received suppressive therapy for extended periods will also finally experience clinically active vivax malaria after protracted incubation periods.

Attention should be directed to what would appear to be a fundamental difference in clinically active vivax infections arising on the one hand as the result of a single inoculation with a single strain of parasites, or on the other as a result of repeated inoculations with numerous strains. The attack arising from autochthonous infections acquired in regions of low endemicity or naturally induced infections are of the first category; those arising after protracted exposure in regions of high or hyperendemicity are of the second. There is a possibility that the representatives of the different strains acquired under the latter circumstances do not simultaneously participate in the initial clinical activity, but may become successively and discontinuously active. In the latter event the various clinical episodes would not necessarily represent a series of recrudescences and relapses in which all strains present participate, but some at least may represent primary clinical activity due to distinct strains operating alone, and various recrudescences and relapses may be due to the reactivation of distinctly different strains.

Impetigo Contagiosa in the Army treated with Microcrystalline Sulphathiazole

By R. M. B. MACKENNA

and

E. S. COOPER-WILLIS

(Abstracted from the *Lancet*, ii, 22nd September, 1945, p. 357)

STATISTICAL analysis of the results obtained in 1,118 uncomplicated cases of impetigo treated in three different ways suggests the following answers to the two questions which the investigation was designed to answer:

Treatment with 15 per cent sulphathiazole administered in either form is significantly better than treatment with lotio cupro-zincica, except for the risk of sensitization in 2½ per cent of cases. The length of stay in hospital under treatment with either form of sulphathiazole is appreciably shorter than with lotio cupro-zincica.

As between the two forms of sulphathiazole, the advantage lies with the microcrystalline form, but this advantage, though probably significant, was outweighed in 1944 by scarcity of supply.

Diodoquin for Chronic Amœbic Dysentery in Service Personnel invalided from India

By T. C. St. C. MORTON

(Abstracted from *Trop. Dis. Bull.*, September 1945, pp. 731-33)

THIS article reports a clinical trial of diodoquin in a series of R.A.F. patients invalided from India for relapsing amœbic dysentery. The majority had

received emetine injections plus carbarsone, stovarsol, sulphaguanidine and sulphapyridine. Three tablets of diodoquin three times a day for twenty days was the standard dose.

Twenty-six cases were treated by diodoquin only, thirty-nine by diodoquin plus quinoxyl retention enemata, thirteen by emetine injection plus diodoquin plus quinoxyl retention enemata, and the fourth series with E.B.I., cleansing bowel washout with bicarbonate, followed by quinoxyl retention enemata, this treatment being followed by carbarsone. There were twenty-four cases in this series.

The results of these cases are discussed and analysed. Two cases of intolerance to diodoquin were encountered in the form of abdominal pain, diarrhoea. The conclusion was that 'diodoquin appears to be the best of oxyquinoline group of drugs in the treatment of amebiasis, and is a valuable addition to the list of remedies'.

The Limitations of Penicillin in Treating Empyema

By J. K. POPPE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 6th October, 1945, p. 435)

1. POTENTIAL empyemas should be treated with large doses of penicillin during their incipient period of development.

2. Patients who have been 'cured' of their empyemas by penicillin should be carefully watched over at least a two-week period for a possible recurrence.

3. Any toxic or non-toxic turbid pleural effusion containing polymorphonuclear cells following a pyogenic infection treated with penicillin should be surgically drained, even though the pus is sterile on culture.

Tolerance to Amino-acid Mixtures and Casein Digests Given Intravenously. Glutamic Acid responsible for Reactions

By S. C. MADDEN *et al.*

(Abstracted from the *Journal of Experimental Medicine*, Vol. LXXXI, 1st May, 1945, p. 439. As abstracted in the *Bulletin of Hygiene*, Vol. XX, September 1945, p. 562)

THIS paper reports tolerance tests to the intravenous injection into dogs of mixtures of aminoacids and of protein digests. It has been found that certain mixtures of crystalline aminoacids are well tolerated, whereas the protein digests must be given slowly to avoid vomiting. Various mixtures of the 10 essential aminoacids given on different days to the same dog, produced vomiting eight times out of 10: similar mixtures to which glycine was added led to vomiting only once in 11 times. These daily injections were sufficient to maintain a positive nitrogen balance for the three weeks of the injections.

Mixtures of these 10 aminoacids plus non-essential aminoacids, exclusive of glutamic acid, were given at rates up to 10 mg. N. per kg. per minute in quantities greater than 300 mg. per kg. without any evident sign of disturbance. The inclusion of natural or racemic glutamic acid in similar mixtures led frequently to vomiting when the rate of administration was greater than 4 mg. N. per kg. per minute. The presence of glutamic acid in the mixture appeared to be of more importance than the rate of delivery. The pH of the mixture was not found to affect the result. Aspartic acid, another dicarboxylic aminoacid, produced no disturbance in the concentration tested: the concentration used was, however, less than that used for glutamic acid. No explanation is offered for the process by which glutamic acid leads to vomiting.

'Anigen' (an enzymatic digest of casein and pork pancreas) and 'Aminoacid Stearns' (an acid hydrolysate of casein fortified with tryptophane) both lead to vomiting when injected at rates above 2 mg. N. per kg. per minute, probably because of their glutamic acid content. There is a suggestion that the enzymic digest is slightly better tolerated than the acid hydrolysate.

No serious reaction occurred as a result of giving any mixture of aminoacid or casein digests.

It is suggested that attention might profitably be given to the preparation of an inexpensive protein hydrolysate of very low glutamic acid content. If this proves impossible, it is hoped that the cost of appropriate mixtures of aminoacids can be reduced.

The Treatment of Actinomycosis with Penicillin

By J. M. WALKER

and

J. W. HAMILTON

(Abstracted from the *Annals of Surgery*, Vol. CXXI, March 1945, p. 373. As abstracted in the *Bulletin of Hygiene*, Vol. XX, August 1945, p. 471)

THE authors describe the successful treatment with penicillin of six cases of actinomycosis, caused, presumably, by the anaerobic type of *Actinomyces* (the fungus was not cultivated). The cases were divided, clinically, into three groups: (a) with only the soft tissues involved (two cases); (b) with both bone and soft tissues involved (three cases); and (c) with generalized systemic disease (one case).

Preliminary treatment, in some cases very brief, with sulphadiazine, sulphathiazole, potassium iodide or x-ray therapy gave little, if any, favourable result. Penicillin was given in 3-hourly doses of 15,000 Oxford units intravenously, but, later, this mode of administration was abandoned and intramuscular injections of 25,000 units at 3-hourly intervals were given instead. All the cases responded favourably, but early apparent cure was, in some, followed by recurrence of the disease, necessitating a further course of penicillin. Prolonged treatment is therefore necessary and the total amounts of penicillin given were 4,300,000 units in the simplest case and 8,170,000 units in the severe generalized case. Whenever practicable, surgical treatment is a valuable adjunct to penicillin therapy.

In the single case of generalized systemic infection (group C), both lungs, the caecum and ascending colon and the right side of the diaphragm were involved; there was a subhepatic abscess and the tissues about the right knee joint were infected. The patient was in a critical state when penicillin treatment was commenced. He was given 15,000 units intramuscularly, at 3-hourly intervals, for about three weeks, the dose at each injection was then raised to 25,000 units for the next three weeks, and reduced again to 15,000 units for the final period of five weeks. Apparent cure resulted and seven months after the completion of the penicillin treatment there was no evidence of recurrence. In the authors' words 'The response to penicillin was brilliant. It was almost unbelievable to see the rapid improvement of this dying man to penicillin therapy'. 'There is little doubt that penicillin is the most effective agent in treatment of actinomycosis.'

Benzyl Penicillin

(From the *Journal of the American Medical Association*, Vol. CXXIX, 20th October, 1945, p. 554)

RESEARCH on penicillin has been pointed toward finding products of maximum clinical efficiency. Tainter and his associates of the Winthrop Chemical Company claim that the benzyl ester of penicillin is sufficiently superior to ordinary sodium penicillin to merit clinical trial. Benzyl penicillin is prepared by treating free

penicillin in an inert organic solvent with an excess of phenyl diazomethane. Any unreacted penicillin is extracted with sodium bicarbonate solution. Evaporation of the solvent yields a resinous product which can be heated well above 100°C. without deterioration. Routine *in vitro* tests against broth cultures of *Staphylococcus aureus* show that this compound is relatively inert, having only one-thirtieth the bacteriostatic titre of sodium penicillin. This inert product, however, is readily activated by the addition of rat kidney extract, rat serum or guinea-pig serum, presumably as a result of enzyme action. One half of the bound penicillin is apparently set free as a result of hydrolytic cleavage. Assuming that a similar hydrolytic regeneration takes place in the animal body, the predictable therapeutic potency of benzyl penicillin would be much greater than that suggested by its low *in vitro* titre. Benzyl penicillin dissolved in a vegetable oil and injected subcutaneously, or given by mouth, was titrated therapeutically on mice inoculated intraperitoneally with multilethal doses of streptococci or pneumococci. Control titres were made with ordinary penicillin. The data thus far obtained show that, when injected subcutaneously, benzyl penicillin has at least three times the therapeutic potency of sodium penicillin. When taken by mouth the therapeutic potency is approximately five times that of sodium penicillin. Given orally, it has substantially the same therapeutic effect as an equivalent weight of sodium penicillin injected subcutaneously. Benzyl penicillin is now being tested on a large scale in clinical cases, and the results will be awaited with much clinical interest.

Fatty Hepatomegaly with Pancreatic Fibrosis controlled by Lipocaic

By L. F. BROWNE

and

W. THOMAS

(Abstracted from the *American Journal of Digestive Diseases*, Vol. XII, July 1945, p. 250. As abstracted in the *Journal of the American Medical Association*, Vol. CXXIX, 15th September, 1945, p. 233)

For the past eighteen months Browne and Thomas have observed a patient who exhibits many of the signs and symptoms of lipocaic deficiency. The administration of lipocaic, furnished by Dr. Dragstedt's laboratory, has produced a striking decrease in the size of the enlarged liver, stabilized the fat concentration of the blood and improved the liver function. There was gain in weight, restoration of appetite and a sense of well-being. The withdrawal of lipocaic has repeatedly caused the re-establishment of the syndrome. The appearance of pronounced fatty infiltration of the liver in this patient together with evidence of extensive fibrosis of the pancreas as revealed at the exploratory operation suggests an inter-relationship between the two phenomena. Exacerbation of the hepatomegaly due to the ingestion of large amounts of alcohol, which occurred several times in this case, is interesting in view of Connor's observations that fatty infiltration of the liver represents an early stage in the development of cirrhosis. The complete recession of the hepatomegaly and striking clinical improvement produced by the administration of lipocaic presents evidence that a deficiency of this secretion due to the fibrosis of the pancreas was the underlying cause of the disease.

Acetylcholine and Paroxysmal Tachycardia

(From the *Journal of the American Medical Association*, Vol. CXXIX, 15th September, 1945, p. 226)

The Belgian Society of Cardiology heard a communication by Segers, J. Lequime and H. Denolin on

the arrest of crises of paroxysmal tachycardia by the intravenous injection of acetylcholine. The acetylcholine was administered intravenously, the dose varying between 0.01 and 0.10 gm. dissolved in a 5 per cent solution. The authors were able to arrest with this method sixty-five attacks of tachycardia in 8 different subjects. There were no failures. The arrest of the attack was always prompt, less than thirty seconds after the termination of the injection.

Disseminated Calcified and Bony Nodules in Lungs associated with Mitral Disease

By A. GRISHMAN

and

I. J. KANE

(Abstracted from the *American Journal of Roentgenology and Radium Therapy*, Vol. LIII, June 1945, p. 575. As abstracted in the *Journal of the American Medical Association*, Vol. CXXIX, 15th September, 1945, p. 234)

GRISHMAN and KANE draw attention to the co-existence of disseminated calcified and bony lesions in the lungs and rheumatic mitral disease. The present report is an attempt to correlate the x-ray, pathologic and clinical findings in 8 cases. The lesion was discovered in 4 cases preceding the first episode of congestive heart failure. The pathogenesis of the pulmonary lesions is not clear. There is no microscopic evidence that pulmonary arteritis or small pulmonary infarctions are precursors of such lesions. They suggest that careful inspection of the lungs in cases of adolescent or preadolescent rheumatic fever may yield significant data. The clinical histories of the reported cases suggest strongly that the precursor to these lesions must appear early in rheumatic fever and probably in childhood. The triad of symptoms that is important in the differentiation from tuberculosis is: (1) the predominantly basal bilateral distribution, (2) the association with evidence of mitral stenosis, and (3) the absence of other evidence of pulmonary tuberculosis.

DDT Water Emulsion in Rice Fields as a Method of Controlling Larvæ of Anopheles Quadrimaculatus and Other Mosquitoes

By F. L. KNOWLES

and

F. W. FISK

(Abstracted from the *Public Health Reports*, Vol. LX, 31st August, 1945, p. 1005)

A METHOD of applying a DDT water emulsion at the pump to flooding waters of a rice field is described. Data obtained from 28,000 dipping records of mosquito larval counts are given according to DDT dosage, solvent used, and position of plot. Larval counts increased with the distance from the pump, indicating a gradual loss in the toxicity of the DDT-treated water as it flowed through the canals and rice fields.

Yields of harvested rice in the DDT-treated 100-acre field were higher than the average or highest yields for previous years, from untreated fields, and indicate that DDT did not injure the growing rice.

Although these results indicate a reduction of mosquito larvæ production by the application of DDT to the flooding water as it enters the rice fields, it is well to note that the production of mosquito larvæ was by no means eliminated.

Spinal Osteoporosis of Unknown Origin

By H. J. BURROWS
and

G. GRAHAM

(Abstracted from the *Quarterly Journal of Medicine*, Vol. XIV, July 1945, p. 147)

1. A SERIES of 20 patients with spinal osteoporosis of unknown origin has been observed between 1939 and 1943.
2. The osteoporosis is most marked in the lower part of the back where secondary deformity of the vertebræ occurs. Patients who did not show deformity of the spine are not included in our series. Pelvic deformity such as occurs in puerperal osteomalacia was absent.
3. The symptoms, signs, and radiological appearances are characteristic.
4. The clinical and pathological changes are different from those of osteomalacia.
5. The possible causes of the condition are discussed, but no one factor can be incriminated.
6. The symptoms can be relieved by treatment, but an increase in the calcification of the affected vertebræ was not demonstrated radiographically.

Intravenous Alcohol and the Surgical Patient

(From the *Medical Press and Circular*, Vol. CCXIV, 19th September, 1945, p. 181)

ALTHOUGH it is a well-known fact that alcohol by mouth is a very useful form of treatment in the very debilitated surgical patient, it has not been known that intravenous alcohol held out good prospects. Moore and Karp of Chicago, experimenting with intravenous alcohol, have come to the following conclusions:—

- (1) Five per cent and 10 per cent alcohol intravenously increases the caloric intake and has special value in those cases with inanition.
- (2) It is a potent sedative and analgesic, and can be substituted for the opiates and other forms of sedation.
- (3) Sedation is not attended with depressed respiration.
- (4) It may be used in cardiac patients with relative safety because of its vasodilatory effect and minimal effect on the blood pressure.
- (5) It has a definite place in regional anæsthesia as a supplement during the operative procedure.
- (6) It has proved its value in alcoholic patients who cannot be controlled with the usual doses of narcotics.
- (7) There are no contra-indications to its use.

The Effect of Topically Applied Sodium Fluoride on Dental Caries

By J. W. KNUTSON
and

W. D. ARMSTRONG

(Abstracted from the *Public Health Reports*, Vol. LX, 14th September, 1945, p. 1085)

DATA on the incidence of dental caries in the permanent teeth of a treated group of children and a control group of children for the second year of a longitudinal study have been presented and analysed. The data for the first study year have been reported previously. During an 8-week period, April and May 1942, the children in the treated group received 7 to 15 topical applications of sodium fluoride solution to the teeth in the left quadrants of the mouth. Analysis of the data indicates:

1. During the 2-year period ending May 1944, 41.3 per cent less teeth became carious of the fluoride-treated than of the untreated teeth of the treated

group of children. The number of additional tooth surfaces which became decayed in teeth which were carious at the beginning of the study was 23.1 per cent less in treated than in untreated carious teeth.

2. During the second study year, the year ending May 1944, 46.6 per cent less treated teeth became carious than untreated teeth. The number of additional surfaces which became decayed in previously carious teeth was 25.2 per cent less in treated than in untreated carious teeth.

3. By and large the findings confirm those reported for the first study year. In addition it is indicated that the fluoride treatments are fully as effective in inhibiting dental caries during the second year following treatment as during the first year. Further, the evidence suggests that the treatment of carious teeth reduces approximately 20 per cent the liability to attack on additional surfaces.

4. The incidence of caries in the permanent teeth of the control group of children, by mouth quadrants, was strikingly similar in the two upper quadrants and also in the two lower mouth quadrants.

The foregoing results of this initial or pilot study on the caries inhibiting effect of topically applied fluorides are sufficiently encouraging to justify additional and more stringently controlled studies. One such study designed to test the relative effectiveness of different numbers of treatments is now in progress and plans for conducting others are being made.

The Control of Rat Fleas (*Xenopsylla cheopis*) by DDT

By D. E. DAVIS

(Abstracted from the *Public Health Reports*, Vol. LX, 4th May, 1945, p. 485)

LABORATORY and field experiments were conducted to eradicate rat fleas (*X. cheopis*) with the insecticide DDT in order to develop an additional method for the control of typhus fever.

Fleas placed in a jar with small amounts of DDT died in 4 hours. Rats were found to be free of fleas after the application of small amounts of DDT to the fur. Rats were captured in buildings before and after the building was dusted with DDT. The number of fleas per rat in 6 stores was 13.9 before dusting and 0.6 a month after dusting. The stores had an index of 0.2 and 0.5 fleas per rat 4 months after dusting.

The use of DDT to reduce the number of rat fleas is a practical procedure which may be useful in control of typhus fever.

Malaria Parasites in Thick Films Stained by Modified Field's Stain. Method of Using Field's Stain

By P. G. SHUTE

(From Transactions of the *Royal Society of Tropical Medicine and Hygiene*, Vol. XXXIX, September 1945, p. 7)

BETWEEN immersion in the azur I methylene blue and the eosin solutions, films are bathed in the isotonic phosphate buffer solution for 1 to 3 seconds instead of in distilled water, as suggested by Field. This removes most of the hæmoglobin without distorting the leucocytes.

Intensification of staining can be obtained by restaining with very weak Leishman. After the film is dry following staining with Field's, one drop of Leishman is allowed to act for 2 or 3 seconds and is then diluted with eight to ten drops of distilled water and stained for a further 5 to 10 minutes. By this double method Schüffner's dots stain prominently, even

in very young ring forms. Counter staining with Giemsa's stain is less satisfactory than Leishman's.

Very thick films.—When films which are very thick (thick drops) are sent to the laboratory, Field's rapid method is unsatisfactory. Such films should be soaked in a jar of phosphate buffer solution until most, but not all, of the hæmoglobin has been dissolved out. The films are then passed through the stains in the ordinary way.

Old thick films.—Films may be stained satisfactorily up to at least 28 days after their preparation if, before being stained, they are soaked in the phosphate buffer solution until the hæmoglobin begins to dissolve out. This may take up to half an hour.

Films adhering to the slide.—Thick films which are stained as soon as they have dried tend to peel off during the process of staining. This can be prevented by passing the films through the flame of a spirit lamp five or six times before staining. Films which are not stained for 24 hours adhere firmly.

At the present time, when the microscopical diagnosis of malaria is being carried out on a very large scale mostly by workers who are neither malariologists nor protozoologists, and the thick film method of diagnosis is in general use, any extra time spent in staining which will enable parasites and the species to which they belong to be diagnosed with accuracy is time well spent. It saves much time during the actual examination of the film both as regards whether an organism is a malaria parasite or not and it also makes species diagnosis easy. Counter staining thick films with weak Leishman's stain following Field's staining is well worth the little extra time involved.

DDT Poisoning

(From the *International Medical Digest*, Vol. XLVII, September 1945, p. 186)

SINCE we discussed the modern methods of destroying insect vectors of disease, much has been written concerning the toxicity of DDT, the most important of the insecticides so far developed. Some apprehension of poisoning in humans was expressed in early writings, although no ill effects of consequence were observed in the many field investigations by the army, during the conquest of typhus in Naples when thousands of humans were deloused every day or in the North African campaign. Nevertheless, further studies were considered desirable and they have been conducted in this country and in England.

The most recent and perhaps one of the most thorough studies has just been reported from England.

Cameron, of the University of London, after experimental investigations on animals together with observations on human subjects exposed for some time to this compound, concurs with the opinion of American investigators, in that there is a wide margin of safety in the use of this very efficient insecticide. He considers that if maximum concentration of 0.5 per cent of DDT be used in sprays, there is no reason to anticipate any danger to man. He contends that even with long-continued exposure to such sprays, it is difficult to see how ill effects would result. He believes that only gross carelessness would likely lead to serious effects. He recommends cleanliness by hand washing or bathing, gloves and protective garments and respirators when spraying concentrated solutions. Most observers agree that anorexia, muscular weakness and fine tremors are early signs of toxicity and if the individual is immediately shielded from further exposure these symptoms clear up quite promptly. In brief, toxic levels are not easily reached if protective measures are used and dilute solutions are employed.

However, with increased use of DDT, carelessness is very probable. Moreover, the use of stronger solutions is sometimes necessary. It is of interest, therefore, to note a treatment which comes from Brazilian investigators. They contend that the symptoms following the administration of DDT are not unlike those of carbon tetrachloride. So, since calcium had proved effective in preventing the effects of acute intoxication by carbon tetrachloride, it was tried for DDT. Dogs were given DDT (100 mg. per kg. body weight) in olive oil daily until intense symptoms of poisoning were observed. It was then found that intravenous injections of 20 c.cm. of a 10 per cent solution of calcium gluconate effected a cure in 2 to 3 hours instead of 12 to 24 hours necessary in the absence of treatment. Furthermore, it was noted that injections of calcium gluconate for several days before DDT was administered greatly reduced the severity of intoxication. The dogs used in the experiments were alive and well a month after the end of the experiments.

From what has been written about the toxicity of DDT so far, the impression is that it really cannot be regarded as a menace to humans. To be sure, it should not be used carelessly and reasonable precautions should be taken just as have always been used with similar preparations. Trained personnel have satisfactorily handled far more dangerous substances and, by following indicated precautions, have reduced hazards to a negligible risk. DDT in the prevention of typhus in Africa and Naples alone demonstrated the benefit that its use is to humanity in an immeasurable way, so it looks as if any discussion of its toxicity is absurd in the light of the evidence so far adduced.

Reviews

ORTHOPÆDIC SURGERY.—By Walter Mercer, M.B., Ch.B., F.R.C.E., F.R.S.E. Third Edition. 1943. Edward Arnold and Co., London. Pp. xi plus 947, with 415 illustrations. Price, 45s. net

PROFESSOR FRASER states in his foreword that the author of this book comes into the category of those men 'who, while practising general surgery, have followed the call of training, of ambition, or it may be, of interest, and have adopted for particular attention and study one special branch in the wide field of general surgical work', orthopædics being his chosen branch. The book has been developed around the nucleus of a series of lectures and clinics given by the author, under the guidance of Professor Fraser, during the last few years, to undergraduates and postgraduates in response to whose request the book has been written.

There are twenty chapters in the book bearing the following titles: introduction, congenital deformities, general affections of the skeleton, affections of bones, tuberculosis of bone, tuberculosis of joints, non-tuberculous affections of joints, chronic arthritis, affections of the epiphyses, paralysis, affections of nerves, circulatory disturbances of the extremities, affections of the spine, affections of the shoulder joint, affections of the knee joint, affections of the foot, some complications of trauma, manipulative surgery, arthrodesis and arthroplasty, and affections of soft tissues. Great attention and care have been devoted to every chapter; all are sufficiently comprehensive and contain the author's considered opinions based on many years of practical experience. Professor Fraser himself testifies to the detail and care bestowed upon every page. The

x-ray pictures presented are excellent and the line drawings done by the author's wife are no less so. We believe with Professor Fraser that 'Mr. Mercer has contributed a most readable and practical treatise on the subject of orthopædics'.

THE TREATMENT OF PEPTIC ULCER.—By George J. Heuer, M.D., assisted by Cranston Holman, M.D., and William A. Cooper, M.D. 1944. J. B. Lippincott Company, London. Pp. vii plus 118. Price, 18s.

DR. HEUER, the head of the Surgical Department associating the New York Hospital and Cornell University Medical College, developed a rather ambitious plan of assembling the results of the activities of the department during its first ten years of existence ending in 1942. Though most of the members of the staff to whom different subjects for investigation were assigned left on was severe, the data for the study of peptic ulcer were fortunately collected, and Dr. Heuer has written this book with these data. The text matter is presented in the form of a series of eleven 'exhibits' giving results of various kinds of treatment of peptic ulcer, comments on these exhibits, comparison of results, effects of gastro-enterostomy and gastric resection on gastric secretion, incidence of malignancy, survey of literature, discussion and summary. During the period under review 1,204 cases of peptic ulcer were admitted into the hospital, the majority of whom were treated medically, and over 90 per cent were followed up successfully by repeated interviews and examinations of the patients at the clinic.

The literature on the subject is thoroughly reviewed and a detailed discussion of the results is presented. Some of the main conclusions of the authors are that they 'should urge surgery more strongly than we have, particularly in those patients in whom hæmorrhage is a prominent feature of their disease and in those with a rapid, progressive course in whom pain and tenderness in the epigastrium suggest the possibility of perforation', and that 'the satisfactory results of gastro-enterostomy and gastric resection on the long or short term of follow-up vary within 10 per cent of each other, gastric resection having the advantage. This advantage however is reduced by the greater immediate mortality of the procedure'.

The authors emphasize 'that the findings in this study and the conclusions drawn from them are almost certain to be changed as time goes on'. This study, therefore, must be considered as an interim report, to be repeated, preferably, when all of the patients included in it have been followed for at least five years'. The ætiologic factors of this disease are obscure and its treatment is unsatisfactory, but this elaborate and thorough analysis of such a large series of cases is naturally of great interest.

BONE-GRAFTING IN THE TREATMENT OF FRACTURES.—By J. R. Armstrong, M.D., M.Ch., F.R.C.S. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. ix plus 175, with 204 illustrations, several in colour. Price, 25s. net

THE author states in the preface that the demands on reparative surgery of the locomotor system have greatly increased in modern times, and that this has led to 'an increased awareness of the vital importance of attention to the many details which can make or mar the final result'. This simple and practical book is an attempt to remedy defects commonly found in standard textbooks, such as lack of space allotted to the application of bone-grafting to the treatment of fractures, curtailed descriptions of operative technique, scanty information regarding pre- and post-operative treatment, and the absence of descriptions of newer procedures.

The general and preliminary aspects of the subject are dealt with in the first five chapters which are entitled: Principles, general indications, contra-indications; types, sources, and fixation of grafts; pre- and post-operative treatment; operative technique; and cutting and preparation of grafts. The remaining

fourteen chapters are on fractures of the spine, the clavicle, the humerus, the radius, the ulna, the radius and ulna, the carpal scaphoid, the metacarpals and phalanges, the neck of the femur, the shaft of the femur, tibia or tibia and fibula, the ankle, the tarsus, and the metatarsals. There is also an appendix giving statistics concerning the incidence of bone-grafting in the treatment of fractures from a Royal Air Force orthopædic centre.

Mr. Watson Jones states in his foreword as follows: 'In his monograph on bone-grafting in the treatment of fractures Mr. Armstrong's work reflects the surgical development of two hundred years—the research of Hunter, the work of Lister, the inspiration of Macewen, the skill of Lane and the craftsmanship of Albee. On this very sure foundation, linked to recent research in metallurgy, is based a technique of bone-grafting which almost completely solves the problem of slow union, delayed union and non-union'. Regarding this technique of onlay bone-grafting with vitallium screw fixation, he gives a warning: 'The surgeon who proposes to adopt the recommendations of this monograph must first achieve so perfect a command of aseptic technique that if, within a few days of operation, the patient develops afebrile reaction he can say with complete confidence: "He may have pleurisy; he may have pneumonia; but whatsoever he has, I am quite certain that he has no infection of the wound"'. The illustrations are numerous and good, and include some in colour, the colour printing being of a novel type. High quality paper has been used and the printing is in bold type and broad-spaced.

A PRACTICE OF ORTHOPÆDIC SURGERY.—By T. P. McMurray, M.B., M.Ch., F.R.C.S. (Edin.). Second Edition. 1945. Edward Arnold and Co., London. Pp. viii plus 435, with 191 illustrations. Price, 30s. net

THE object of this book is to present the basic principles underlying treatment in orthopædic surgery to the final year student and the young surgeon. The text matter consists of twenty-five chapters. The first three chapters entitled orthopædic surgery, splints and apparatus, and rigidity of joints are introductory and preliminary. Disorders of the knee and shoulder joints are dealt with in chapters IV and V. The sixth chapter discusses the general aspects of tuberculous affections of bones and joints and is followed by separate chapters on tuberculosis of the hip joint, knee, ankle and tarsus, spine and sacro-iliac joint, and shoulder, elbow and wrist. The other chapters are on chronic arthritis, epiphyseal affections, non-tuberculous affections of the spine, lateral curvature of the spine, acquired deformities, the foot, acute anterior poliomyelitis, spastic paralysis, peripheral nerve injuries, affections of muscles and tendons, congenital dislocations and deformities (two chapters), rickets, general affections of bone, and tumours of bone.

The treatments described are those that the author believes to have given the most consistently satisfactory results and bear a conservative outlook. Extensive bone operations which must interfere with growth are not favoured. Fractures and their treatment are omitted. The x-ray and other illustrations given are good, and the book is a very sound and helpful one.

THE TREATMENT OF ACUTE INTESTINAL OBSTRUCTION.—By Judson T. Chesterman, M.R.C.P., F.R.C.S., F.A.C.S. 1945. J. and A. Churchill Ltd., London. Pp. viii plus 116, illustrated. Price, 10s. 6d.

In the preface it is stated that this book 'is an attempt to state the treatment of acute intestinal obstruction based on extensive reading of the subject, experimental work, and the treatment of more than five hundred cases. The author has also the advantage of first hand study in both British and American hospitals of the methods of treating the condition'. The attempt is carried out in a systematic manner; the book is in two parts; part I entitled 'general considerations' deals with the pathology induced by acute

intestinal obstruction and by its release, diagnosis, adjuvant measures, suction treatment, and operative treatment; part II entitled 'discussion on special obstructions' classifies and discusses the special obstructions under mechanical, vascular, and neurogenic ones; the mechanical obstructions are discussed in great detail. An excellent presentation of the subject.

SURGICAL NURSING AND AFTER-TREATMENT.—

By H. C. Rutherford Darling, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.F.P.S. (Glas.). Ninth Edition. 1946. J. and A. Churchill Ltd., London. Pp. x plus 694, with 211 illustrations. Price, 12s. 6d.

SOME of the previous editions of this treatise have been reviewed in this journal; the eighth one was reviewed in 1945. In the present edition the work has again been revised and some practical suggestions have been included.

THE PREMATURE BABY.—By V. Mary Crosse, M.D.

(Lond.), D.P.H., M.M.S.A., D.R.C.O.G. 1945. J. and A. Churchill Ltd., London. Pp. viii plus 156, with 14 illustrations. Price, 10s. 6d.

PREMATURE birth with its attendant high infant mortality is one of the outstanding health problems in India to-day and though the problem in India is largely one of maternal malnutrition during pregnancy, much could be achieved by unremitting care of the premature infant. Dr. Mary Crosse, Chief Obstetric Officer in charge of the Birmingham Maternity Homes and Premature Baby Unit, has for 14 years studied the latter problem, and by methods described in her book has achieved results far in advance of anything previously accomplished in the United Kingdom. The general management of the premature baby in an institution or at home, clothing and feeding are described with meticulous attention to detail, and the book should prove invaluable to all members of the medical and nursing professions whose field of work covers the care of the newborn infant. Interesting statistical tables are given in the final section of the book, and a comprehensive and detailed review of the complications liable to occur in the premature complete this exhaustive study of the premature baby and his care.

J. M. O.

CHEST EXAMINATION.—By Richard R. Trall, M.C., M.A., M.D. (Aberd.), F.R.C.P. (Lond.). Second Edition. 1945. J. and A. Churchill Ltd., London. Pp. x plus 122, with 94 illustrations. Price, 12s. 6d.

THE previous edition of this book was reviewed in this journal in 1944 and it was pointed out that 'the discussion of some points is too brief to be of much value'. In the present edition notes have been added on such points as the interpretation of breath sounds and the 'normal abnormalities' of the bony thorax. Additional illustrative x-rays have been set in the text. As mentioned in our last review, the book is valuable from the point of view of the study of physical signs of chest diseases.

ESSENTIALS OF INDUSTRIAL HEALTH.—By C. O. Sappington, M.D., Dr.P.H. 1943. J. B. Lippincott Company, London. Pp. xii plus 626, with 63 illustrations. Price, 42s.

As the author states in the preface it is only through industrial health that the desire of the employer to proceed at peak production under all conditions and the desire of the employee to continue to draw maximum wages can be accomplished. The medical schools in the U.S.A. are now placing more emphasis on the fundamentals of industrial health in undergraduate and graduate courses, and this book closely follows a recently proposed course for undergraduates.

The book consists of fifteen chapters divided into three parts, each part containing five chapters. The first part on industrial health administration contains chapters entitled origin and later development of industrial health, occupational morbidity and mortality,

distribution of industrial health service, classification of industrial physicians, and the industrial medical department. The second part entitled 'industrial hygiene and toxicology' contains chapters on industrial health exposures, the plant survey, plant sanitation and hygiene, personal hygiene for workers and co-ordination of industrial and community health services. The third part on industrial medicine and traumatic surgery has chapters on the worker and the job, industrial accidents, occupational diseases, non-occupational disabilities, and workmen's compensation and rehabilitation. There are, in addition, several appendices giving valuable information and guidance for industrial health programmes.

In the preparation of this book numerous authoritative publications of the U.S.A. and Great Britain have been consulted and no effort has been spared to make a comprehensive and standard textbook on the subject. The book therefore deserves to be widely read in a country such as India where industry is still in the process of development.

OLD AGE: SOME PRACTICAL POINTS IN GERIATRICS.—By Trevor H. Howell, M.R.C.P.

(Edin.). 1945. H. K. Lewis and Co., Ltd., London. Pp. vi plus 50. Price, 4s. 6d.

THIS small book is based on the author's clinical experience at the Royal Hospital, Chelsea, and as indicated by the sub-title, is devoted to a brief description of the practical problems in the care and treatment of the aged. It contains ten chapters mainly dealing with their comfort and management, normal physiology of old age, and certain diseases common at this period of life. The book is very practical and should stimulate practitioners to take more interest in these people who deserve as much care as those of younger age.

EXTENSILE EXPOSURE APPLIED TO LIMB SURGERY.—By Arnold K. Henry, M.B., M.Ch., F.R.C.S.I. 1945. E. and S. Livingstone Ltd., Edinburgh. Pp. v plus 180, with 127 illustrations. Price, 30s. net

THIS book, states the preface, 'seeks to enlarge the scope of certain set and parcelled methods of approach' to exposures in connection with limb surgery through means 'in which my confidence has grown from using them myself and watching others try them'. Five different exposures of the upper limb, posterior humoral, anterior humoral, the forearm from front, the back of the forearm, and two linked approaches in the hand, and nine of the lower limb, sub-gluteal, of the femur, popliteal, the back of the thigh and the leg, the mid-line popliteal route, posterior exposures in the leg, transition from back to front, the fibula and the peroneal nerves, and plantar exposure, are described. Bone wherever possible is made the core of each exposure. The book, though written in a strong literary style, attempts to get at the anatomy of the parts as accurately as possible with the aid of excellent illustrations.

THE COOKERY BOOK FOR DIABETICS.—Compiled by the Diabetic Association, London. 1945. H. K. Lewis and Co., Ltd., London. Pp. vii plus 74, illustrated. Price, 4s. net

THIS booklet has been compiled by the Diabetic Association of England, and is intended for the diabetic patient. Professor Mottram in his foreword states that 'I am neither a diabetic nor a cook, but if anything could reconcile me to being either, or both, it would be just this book'. Various recipes of soups, egg dishes, meat dishes, fish, vegetables, sweets, savouries, salads, cakes and biscuits, drinks, preserves, pickles, and breakfast dishes are given. Every recipe gives the weights of carbohydrates, proteins and fat in the dish. Food values are pointed out and the cooking of food is described from the point of view of the diabetic's health. Weights and measures and food tables are given at the end. The information given in the book has been carefully checked by experts, and the book can be recommended.

BOOKS RECEIVED

1. Statistics of hospitals and dispensaries in the Punjab for the year 1944. Printed by the Superintendent, Government Printing, Punjab, Lahore. Price, As. 12.
2. Report on soya bean. By the Soya Bean Subcommittee of the Nutrition Advisory Committee, Indian Research Fund Association. January 1946. Page 35. Price, As. 8.
3. An index to rural medical practice. By A. T. W. Simeons, M.D. Pp. 181 plus 10. Kolhapur Government Press. 1945.
4. Research in medicine and other addresses. By Sir Thomas Lewis. Second edition. Pp. x plus 102. H. K. Lewis and Co., London. Price, 5s.
5. Feeding the worker. Canteens in industry. No. 7, March 1946. Government of India, Department of Food, Department of Labour, New Delhi.
6. Nutrition, Bulletin Nos. 15 and 16, April 1946. Department of Food, Government of India, New Delhi. Price, As. 4 each.
7. British policy in Eastern Ethiopia and Eritrea. By Sylvia Pankhurst. Published by the author at 3 Charteris Road, Woodford Green, Essex, England. Price, 1s. each.

Abstracts from Reports

THE MISSION TO LEPERS: A REPORT OF THE SEVENTY-FIRST YEAR'S WORK IN INDIA AND BURMA, FROM SEPTEMBER 1944 TO AUGUST 1945

THE report surveys the year's work in the provinces and the Indian States. At the end of 1944, there were 8,761 inmates under treatment at the various Homes, of whom 2,989 showed marked improvement. The number of outpatients were 12,673. Though the cost is increasing, the Mission is considering plans for extension of work in several areas. The report is illustrated with several photographs which give an idea of its activities and the good work it is doing.

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR M. S. CHADHA is appointed Assistant Chief Health Officer, Delhi Province, with effect from the 5th November, 1945.

Major M. H. Shah, Additional Civil Surgeon, Delhi, is appointed until further orders, to hold collateral charge of the post of Medical Superintendent, Irwin Hospital, New Delhi, with effect from the afternoon of the 5th November, 1945.

Major J. D. Grant, an Agency Surgeon, is posted as Agency Surgeon, Gilgit, with effect from the forenoon of the 1st December, 1945.

The services of Major G. E. S. Stewart, Senior Medical Officer, Port Blair, are replaced at the disposal of the War Department, with effect from the forenoon of the 5th January, 1946.

PROMOTIONS

INDIAN MEDICAL SERVICE

Captains to be Majors

M. C. L. Smith, M.C. Dated 31st October, 1945.
1st November, 1945

V. D. Gordon. S. Shone.
D. R. Nicol. C. H. Bliss.
J. H. Walters.

R. L. Soota, M.B.E. Dated 10th October, 1945.
M. Shankhla. Dated 11th October, 1945.

S. A. Mian. Dated 29th October, 1945.
M. S. Zan. Dated 4th December, 1945.
K. S. R. Menon. Dated 13th December, 1945.
D. R. Cattanch. Dated 28th December, 1945.

RELINQUISHMENTS

The undermentioned officer is permitted to relinquish his commission, and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Ty. Lt.-Col. P. A. Mathew. Dated 19th March, 1945.

The undermentioned officer is permitted to relinquish her commission, and is granted the honorary rank of Captain.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain (Mrs.) R. Puri. Dated 17th November, 1945.

The undermentioned officer is permitted to relinquish his commission on release from Army Service, and is granted the honorary rank of Captain.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain L. B. Belkhode. Dated 10th December, 1945.

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Original Articles

TROPICAL ULCER IN THE HISSAR DISTRICT OF THE PUNJAB

By TRILOKI NATH, M.B., B.S., D.T.M.

Assistant Surgeon, Civil Hospital, Sirsa

IN their book on tropical medicine Rogers and Megaw mention about the occurrence of tropical ulcer in the humid climate of Assam and South India. Cases have also been reported from many other parts of the country, but not so far from the Punjab.* This paper is based on a clinical observation of 60 cases of tropical ulcer occurring in the Hissar district of the Southern Punjab, where the climate is dry with little rainfall and the soil is mostly sandy.

Ætiology.—The following points were noted:

(1) The ulcers were found generally in children and adolescents up to the age of 18, and were not common later. (2) They were mostly found in the poor class of patients who were subjects of malaria, anæmia, avitaminosis or malnutrition. (3) Cases began to appear in the months of September, the number increased in October, November and December and started falling in January. (4) Trauma played a definite part in the ætiology of the ulcer, and most of the patients gave the history of a small abrasion to begin with or an insect bite which was scratched by the patient. Some patients stated that the lesion began as a small vesicle. (5) The ulcers were generally found on the lower extremity below the knee while a few had them on the hands and forearms, but not elsewhere. This shows that to begin with there is a minor abrasion which is more likely to occur on the lower extremity and which later on gets contaminated with dust and dirt.

Clinical picture of the ulcer.—In the earliest stage a small painful vesicle is seen to occur generally on the lower extremity, and on taking its top off thick yellow pus is found underneath. If left at this stage, the discharge gradually increases and the top breaks, resulting in an ulcer which becomes larger and more painful. It assumes generally a circular or oval appearance. The margins are clear cut. On the base there are red granulations. If the ulcer is neglected it becomes bigger and deeper, and the granulations become bigger and unhealthy. There is a considerable amount of disability due to pain and swelling.

Microscopical findings.—Smears made of the scrapings of granulations showed numerous fusiform bacilli in all cases and spirochætes in a few.

Treatment.—The ulcers of 20 cases were scraped initially, later on 5 per cent copper

sulphate dressings were applied. An equal number of cases was dressed with sulphonamide powder after scraping. There was no appreciable difference in the healing time in the two categories. Ambulatory cases took more time to heal up than those which were admitted into the hospital and got proper rest. Twenty patients were treated by strapping with leukoplast. The leukoplast was left undisturbed for at least 10 days in spite of the foul-smelling discharge which accumulated under it, and which seemed to be helping in the healing of the ulcer. These cases did remarkably well and the ulcers healed up in 15 days, whereas with copper sulphate and sulphonamide treatment the average time taken to heal was 35 days. The accompanying conditions, e.g. malaria, anæmia and avitaminosis, were also treated (simultaneously with quinine, cod-liver oil, milk and fresh fruits).

An observation.—While searching for marks of identification on the body of medico-legal cases I have noticed circular and oval scars in a number of cases occurring generally on the lower extremity. One may therefore presume, if not conclude, that the ulcer has been occurring in the district for a number of years and is not a disease recently introduced.

My thanks are due to Dr. Diesh, Civil Surgeon, Hissar, for his kind permission to publish this paper, and his valuable guidance, and to Dr. A. N. Goyle, Pathologist to the Government of Punjab, for the microscopical examinations.

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ULCUS TROPICUM IN FAZILKA (PUNJAB)

By PRAN NATH LUTHRA, M.B., B.S. (Pb.), D.T.M. (Cal.)

Assistant Surgeon, Civil Hospital, Fazilka

THAT this disease which in India had so far been prevalent in the province of Assam has already invaded the provinces of Bombay, Madras, Bengal and United Provinces is evident from recent reports in the *Indian Medical Gazette*.

That the Punjab has formed no barrier to the disease is indicated by this report.*

* See also paper on 'Ulcer tropicum in Fazilka (Punjab)'.—Editor, *I.M.G.*

* See article on 'Tropical ulcer in the Hissar district of the Punjab'.—Editor, *I.M.G.*

The disease was found assuming a mild epidemic form in Fazilka soon after the unusually heavy rains in 1944. Although only 106 cases were seen in the out-patient department and 28 were hospitalized between the middle of August and end of December 1944, the actual figures must have been higher as certainly many cases fail to seek hospital aid.

A milder epidemic was also noticed after the summer rains in 1945. The largest number of cases were seen in the two months immediately following the rains and with the approach of midwinter the cases quickly dwindled.

Fazilka is a small town in the Ferozepore district of the Punjab and is an important centre for wool. It has a population of about 26,000, an annual average rainfall of about 10 inches, and a climate very hot and dry in summer and cold and dry in winter. The rainfall at Fazilka in 1944 was about 16 inches as compared with about 10 inches in 1943 and 12 inches in 1945.

Almost all the patients were drawn from the poor classes and looked malnourished and anæmic. Two of the cases although belonging to a fairly rich family had poor dietary habits and looked no better in development than the cases from the poorer classes.

Eight out of the 28 indoor cases showed enlarged spleen and marked anæmia. All of them admitted that they had access to very little or no milk and had seldom taken any fruits.

Clinical picture.—The ulcers were invariably situated on exposed parts of the body, most commonly below the knees. Forearm, hand and nailbeds were involved in a few cases and then only in the females. The ulcers were usually round or oval varying in size from $\frac{1}{2}$ inch to $3\frac{1}{2}$ inches in diameter. One of the ulcers was 10 inches by 5 inches occupying the dorsum of the foot and the outer aspect of the ankle. The edges of the ulcers were indurated, undermined and raised above the surface. Oedema of the surrounding tissues was evident in some cases. Greyish-yellow sloughs and an offensive sero-sanguineous discharge characterized the ulcers so much so that once recognized the cases could be easily spotted from their characteristic smell. Most of the ulcers were deep in the sub-cutaneous tissues while muscles and tendons were seen under the larger ones. Bone was not reached by any of the ulcers seen by me. Pain and tenderness were constant features. The cases were generally 2 to 3 weeks old when first seen. Ulcers were usually single but in four cases multiple ulcers were seen. In these the ulcers were generally bilateral and in only one case three ulcers were seen on the same leg.

The ulcer usually started as a small blister after some sort of trauma. History of the following kinds of trauma was elicited: (1) Mosquito bites. (2) Minor scratches and abrasions. (3) Small old wounds. (4) Leech bite in one case.

In one medico-legal case a superficial linear incised wound developed into a typical round ulcer. Two cases of ulcers over the inner maleolar regions during their hospitalization developed second ulcers on the contra-lateral inner ankle regions.

In these the ulcers started as small mosquito bites which developed into small blisters, grew in size in a couple of days, burst and gave rise to ulcers that rapidly acquired typical shapes.

Corresponding lymphadenitis was not seen in any of the cases nor were constitutional disturbances present.

Age incidence

5-15 years	15-30 years	30-40 years	40-50 years	Total
59	36	1	10	106

Sex.—Of the 106 cases only 10 were females.

Occupation.—Malnourished children of school-going age born of poor parents, bullock-cart drivers and labourers comprised the majority of cases. Patients were used to walking bare-footed in almost all the cases. Their dietetic habits revealed a gross inadequacy of milk and fruits in their menu. They lived in unhygienic surroundings.

Laboratory findings.—Out of the 115 slides examined with Leishman stain, fusiform bacilli and slender spirochaetes were seen in 81. Fusiform bacilli alone were seen in 34.

In a few atypical cases pyogenic organisms only were seen.

Dr. D. N. Roy of the Calcutta School of Tropical Medicine, who has worked on these ulcers in Assam, very kindly examined a few of the slides for me and confirmed the findings.

A peculiar feature was the absence of micro-organisms in the fluid withdrawn from the blisters of the two indoor cases in which typical ulcers formed later on at those sites.

Leishmania tropica was not met with in the fluid aspirated from margins of the ulcers and the base of the ulcers.

Wassermann reaction was negative in all cases from which blood was sent for examination.

Culturing facilities for studying the morbid anatomy were not available at Fazilka.

Animal experiments.—Two dogs were scarified on the legs and inoculated with discharges from the ulcers. The dogs failed to catch the disease.

Treatment.—Average stay of the hospitalized patients was 14 days under the following treatment:—

1. Complete rest.

2. Cleaning the ulcers daily with a solution of copper sulphate 3 drachms and carbolic acid 1 drachm in 1 ounce of water and dressing with boro-iodoform.

Half the patients were treated by dressings with magnesium sulphate and sulphonamide powder in equal parts.

Their average stay was 20 days.

Penicillin dressings were tried in one case only but there was no acceleration in clearing up of the ulcers with this.

Conclusions.—Presence of tropical ulcer has not hitherto been reported from the Punjab. The clinical description and the bacteriology of the ulcers leave hardly any doubt as to the identity of the condition.

The rôle of the fusiform bacilli and spirochaetes in the causation of this disease is so far unsettled* although evidence in support of their pathogenicity has been advanced now and then. The absence of these organisms from the smears made in the blister stage of the two cases mentioned, indicates that they are perhaps secondary invaders. Dr. Roy working in Assam on these ulcers also attributed a secondary rôle to these organisms.

That the disease which according to most of the observers (Rao *et al.*, 1945; Roy, 1939; Panja and Ghosh, 1944) is a disease of the poor and the ill-nourished may still further spread and assume severe epidemic form under the onslaught of famine, and food shortage threatening India must be seriously considered by the medical profession and the health authorities. The recent spread in places hitherto unaffected should be a sufficient warning.

That no treatment is satisfactory makes the problem still more serious.

Summary

1. One hundred and six cases of tropical ulcers have been reported from the Punjab where the disease had not hitherto been reported.

2. Fusiform bacilli and spirochaetes appear to be secondary invaders.

3. The possibility of the disease assuming an epidemic form under the threatening famine in India is predicted.

Acknowledgment

I am grateful to Dr. D. N. Roy for his very kindly lending me the use of his thesis on 'Tropical ulcer'.

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* The pathogenesis of Naga sore has been discussed in a paper entitled 'Ætiology and treatment of ulcus tropicum', by G. Panja, in the *Ind. Jour. Med. Res.*, **33**, 1, May 1945.—EDITOR, *I.M.G.*

TEN CASES OF TYPHUS IN CIVILIANS IN CALCUTTA

By JOHN LOWE, M.D. (Birmingham)

(From the School of Tropical Medicine, Calcutta)

It was in 1942 that the attention of the writer was first drawn to the occurrence of a fever of the typhus group in and around Calcutta. It was then that a small outbreak occurred in a group of Greek sailors staying on shore in an area not far from the port of Calcutta. Details of this outbreak have not been published.

In 1943 the writer saw a considerable number of cases of typhus in military personnel in the Calcutta area. These cases occurred in both Indian and British troops. It was noticeable that most of the cases were of the nature of scrub typhus, showing agglutination of proteus OXK in the Weil-Felix test, but there were some cases showing OX19 agglutination suggesting murine typhus, and also one or two cases giving agglutination with OX2 suggesting tick typhus.

Thus this experience showed that typhus fever in and near Calcutta was not uncommon; nevertheless cases in the civilian population were not encountered at this time.

The medical literature however does indicate that the fever of the typhus group has probably occurred in Calcutta for many years. In 1912 Bradley and Smith recorded a suspected case of typhus in a British sailor in Barrackpore 15 miles from Calcutta. In 1924 Basu described fifteen cases of typhus-like fever occurring in Calcutta. Boyd (1935) and Wilson (1935) reported a few cases in the army, apparently contracted in the Calcutta area.

We were therefore on the look out for cases of typhus in the civilian population during the period from 1942 onwards when numerous cases were being seen in the area in military personnel. In the School of Tropical Medicine, Calcutta, only one case was seen by Dr. P. C. Sen Gupta in 1944. Roy (1946) recorded two cases seen in Calcutta in August 1944. In 1945, however, ten cases of typhus were seen and admitted into the hospital attached to the school. These ten cases form the basis of the present report.

The best available clinical description of typhus in the Calcutta area so far available is that published by Lusk in 1945.

He described 114 cases seen in military personnel in Calcutta, 54 of these actually arising in the Calcutta area itself and 60 coming from a village about 80 miles from Calcutta. Nearly all these cases were seen during the period July to December. Of the 54 cases seen in the Calcutta area, 42 showed OXK agglutination, 8 OX19, and 1 OX2, and in 3 others the diagnosis was made clinically or at post mortem. The mortality in the 54 Calcutta cases was 20.3 per cent. Lusk gave a good description of the clinical features of the disease which corresponded with descriptions of scrub typhus seen elsewhere. Notable features however were the absence of the eschar at the site of the bite and the absence of local or general lymphadenitis as are commonly recorded in scrub typhus. (These findings were

TABLE

No.	Sex and age	Day of admission	Fever	Toxæmia	Rash	Pain	Throat	General adenitis	Lung signs	Nervous manifestations	Pulse	B.P.	W.B.C. (maximum)	Well-Felix
1	Male, 53 yrs.	10th	Irregular always within 102°F. —32 days.	Severe and persistent.	Very severe petechial and persistent staining.	Severe in head, back and throat.	Intensely congested.	Nil	Bronchitis and broncho-pneumonia.	Apathy, deafness, hoarseness, hiccough, disurea.	Rapid, soft and extra systoles.	108/72	22,000 (during broncho-pneumonia).	OX19 } 1/400 OX2 } on 17th day.
2	Male, 19 yrs.	9th	Remittent max. 103°F. —15 days.	Slight	Nil	Slight	Slightly congested.	Nil	Slight	Apathy, disurea.	Brady-cardia.	..	7,800	OX19 1/400 on 13th day.
3	Female, 18 yrs.	8th	Remittent —15 days.	Slight	Nil	Moderate in head and back.	Slightly congested.	Nil	Slight	Slight	Slight brady-cardia and extra systoles.	105/65 (on admission), 90/50 (on 15th day).	4,600	OX19 1/400 on 19th day.
4	Male, 40 yrs.	9th	Remittent —14 days.	Nil	Nil	Severe in head.	Moderately congested.	Nil	Slight	Slight	Normal	..	8,600	OX19 1/1,600 on 17th day.
5	Male, 47 yrs.	Before the onset of fever.	Continuous max. 103°F. —15 days.	Slight and brief.	Nil	Moderate in head and body.	Moderately congested.	Present	Slight	Slight	Slight brady-cardia.	98/62	11,500	OXK 1/800 on 23rd day.
6	Male, 36 yrs.	6th	Remittent max. 105°F. —14 days.	Moderate	Generalized petechial.	Moderate in head and loins.	Intensely congested.	Nil	Bronchitis	Dullness and apathy.	Normal	..	6,720	OXK 1/100 on 26th day.
7	Male, 20 yrs.	10th	Continuous —18 days.	Slight	Nil	Moderate in head, neck, joints and throat.	Moderately congested.	Nil	Slight	Slight meningismus.	Dicrotic	110/70	5,800	OXK 1/800 on 27th day.
8	Male, 50 yrs.	11th	Remittent —21 days.	Severe	Nil	Moderate in head, neck and body.	Slightly congested.	Nil	Basal congestion.	Marked meningismus, delirium in continence, disurea.	Normal	95/70	6,000	OXK 1/100 on 16th day.
9	Male, 32 yrs.	10th	Continuous max. 101°F. —14 days.	Slight	Nil	Slight	Slightly congested.	Nil	Slight	Dullness, apathy, deafness.	Normal	..	6,500	OX2 1/200 on 16th day.
10	Male, 36 yrs.	10th	Continuous max. 103°F. —died on 15th day.	Profound	Slight blotchy rash on body.	Severe in abdominal wall (hæmorrhage).	Intensely congested.	Present	Patchy consolidation on 13th day.	Dullness, apathy, deafness, hiccough and disurea.	Rapid and irregular with extra systoles.	88/60	17,000 (during bronchitis).	OX19 1/25 on 14th day. Died on 15th day.

Murine

Scrub typhus

Tick typhus

Doubtful

however recorded in the typhus outbreak in the army in the Assam-Burma frontier area.) The rarity of the rash was also recorded by Lusk.

The ten civilian cases seen here in 1945 are here discussed. The first case in the present series was seen at the beginning of October 1945 and during the next few weeks no less than ten cases were admitted to our hospital. They were admitted rather late in the fever, between the 6th and the 10th day, except for one patient who was admitted for another complaint and started his typhus fever two or three days after admission. All the main clinical points regarding these ten cases are recorded in the accompanying table.

A rather curious fact not brought out in the chart is that two of the ten patients were doctors, that three others were servants in the medical college group of hospitals, Calcutta, and one was the servant of a medical man living in Calcutta. It is not suggested that the medical profession and their associates are exposed to typhus infection more than others, but they are perhaps more likely to get admission to hospital when they fall ill. These facts suggest that typhus fever is much more widespread in the general population in Calcutta than has been realized.

Regarding the circumstances having a bearing on infection, the following facts may be quoted: Six of the ten patients were living in the centre of Calcutta with no particular factor increasing the possibility of infection. Only two of the ten cases lived in a village outside Calcutta in rural surroundings. One other patient, a doctor, was residing in Calcutta but went fishing at weekends in the Barrackpore area and was possibly infected there, and one other, a resident in Calcutta, had travelled recently to and from Bombay.

Regarding the facts quoted in the table the following points may be mentioned:

In the nine patients who recovered, the fever lasted 14 or 15 days in six cases, the fever in the other three cases lasting 18, 21 and 32 days. In the latter cases the fever was prolonged by lung complications.

Of the ten cases, four showed definite agglutination with proteus OXK, and were cases of scrub typhus; three agglutinated OX19 and were cases of murine typhus; one agglutinating OX19 and OX2 also was probably murine typhus; one agglutinating OX2 only was possibly tick typhus. In one other case with death on the 15th day, no definite agglutination was obtained (only OX19, 1 in 25). In the cases of scrub typhus, OXK agglutination was late in appearing, and the titre continued to rise after the fever had ended in three out of the four cases.

In only two of the cases was a definite rash seen, and in both of these the rash was petechial.

In no case was a local eschar seen or a localized lymphadenitis. Two cases presented a slight but definite general enlargement of the lymph nodes.

A constant finding in almost all cases was marked congestion of the throat. In four of the cases, lung signs were marked, but slight bronchitis was seen in most of the cases.

Cerebral manifestations were present in most of the cases and marked in several. In severe cases, mental apathy, dullness, deafness, sometimes delirium were seen. A persistent hiccough was seen in two cases. Difficulty in passing urine was seen in four cases.

Signs of cardiac involvement were present in several cases, particularly the severe ones, the pulse becoming rapid, and irregularity and extra systoles appearing. In the milder cases, bradycardia was seen sometimes.

The white cell count was usually only moderately raised except in two cases, both with pneumonia.

The one fatal case was a curious and interesting one. The clinical picture was that of severe typhus, but no agglutination was obtained before death on the 15th day. On admission on the tenth day the patient complained of severe pain in the lower abdomen on the left side, and a definite hard swelling appeared which was diagnosed clinically as a hæmorrhage in the rectus sheath and this was confirmed after death. No hæmorrhages were seen elsewhere however.

Death occurred in only one case out of ten. On the whole, in the ten cases, three could be classed as severe, one as moderately severe, and the rest as slight. A striking feature of the convalescence of the patients who recovered was the general asthenia following this infection. It is obvious that the period of convalescence after typhus, even mild typhus, should be prolonged. There was definite evidence of myocardial changes even in those patients who did not appear to have been seriously ill.

No further case of typhus has been seen since December 1945 (written 1st April, 1946). It will be interesting to see if further cases are encountered in the second half of this and coming years.

Summary

1. Although numerous cases of typhus had been seen in military personnel in Calcutta, recorded cases in the civilian population have been few. The season for typhus in Calcutta is the second half of the year.

2. Ten civilian cases seen in the last quarter of 1945 are described.

3. Four cases were of scrub typhus with OXK agglutination; four were of murine typhus with OX19 agglutination; one case showed OX2 agglutination; one showed no significant agglutination before death.

4. Of the ten cases, three were severe, with one death. The rest were mild and recovered, but convalescence was prolonged.

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Later note.—After several months with no cases of typhus seen, the first case of 1946 has just appeared in our hospital, a mild case of scrub typhus, in May 1946.

OBSERVATIONS ON THE TREATMENT OF 25 CASES OF KALA-AZAR WITH STIBATIN (SODIUM ANTIMONY GLUCONATE) * †

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Introduction.—Kala-azar is endemic in Assam and its periodic recrudescence is well recognized. Such recrudescence has been in evidence since 1943. My attention was drawn in the latter months of 1943 by some of my assistants to some cases of chronic and obstinate intermittent fever which did not respond to any of the anti-malarial drugs. A few of these presented the striking appearances of kala-azar, and many of them were diagnosed as such by various tests mentioned in the body of this paper and summarized in the protocol. Urea stibamine was the only drug that had to be taken recourse to as neo- and solu-stibosan (the former favourites) were not available in the market. Urea stibamine has to be administered intravenously and at times causes severe toxic reactions and, as such, small children, corpulent subjects and patients suffering from general anasarca, not an uncommon condition associated with kala-azar, could not be treated with urea stibamine. At the Annual General Meeting of the Assam and Northern Bengal Branch of the British Medical Association that was held in Shillong in November 1943, Shortt read an interesting paper dealing with the history of researches on kala-azar in Assam and in the discussions that followed Burke and Chakravarty (1944) of Mangaldai Medical Association described the most encouraging results they had obtained with stibatin which, they said, was remarkably non-toxic and could be administered both by the intramuscular and the intravenous routes.

The drug.—Stibatin or sodium antimony gluconate is a pentavalent antimony compound

prepared by Messrs. Glaxo Laboratories and was originally issued in phials each containing 30 c.cm. of a sterile solution with 20 mg. of pentavalent antimony per c.cm.

Patients.—All the 25 patients were labourers belonging to three different tea gardens and were treated under the direct supervision of the writer.

Sex.—Twenty were males and 5 females.

Age.—Their age distribution was between 10 and 50 years, 11 of them being from 10 to 20 years. The duration of illness varied from six months to two years.

Diagnosis.—The diagnosis was based on (i) positive aldehyde reaction, (ii) positive urea stibamine test and on (iii) the demonstration of parasites in spleen or sternal puncture smears.

The findings are tabulated below :—

TABLE

	Total	+ive	—ive
Aldehyde reaction ..	25	25	0
Urea stibamine test ..	25	25	0
Spleen puncture smear ..	21	21	0
Sternal puncture smear ..	4	4	0

Hæmoglobin.—The hæmoglobin percentage was estimated by Tallqvist's scale once before the treatment was commenced and once again on the completion of the treatment. The lowest hæmoglobin before treatment was 30 per cent and the highest 55 per cent, and the average was 43 per cent approximately.

Leucocytes.—Leucopenia was typical in every case. In 5 cases the leucocyte count was below 2,000 per c.mm., in 14 it ranged between 2,100 to 3,000 per c.mm., and in 6 between 3,100 and 4,000 per c.mm.

Spleen.—Enlargement of the spleen was noticeable without exception in the majority of cases varying from 3 to 7 inches below costal margin.

Treatment.—The specific treatment was started as soon as the diagnosis was established. Treatment of a few cases which had mild ascites and albuminuria had to be put off for a few days till the fluid in the abdominal cavity and the albumin in urine disappeared after alkaline diuretics orally. The drug was administered intramuscularly in 16 and intravenously in 9 cases. Treatment for any concomitant infection was carried out and hæmatinics were administered. Case 5 (see protocol) deserves special mention as the girl had been suffering from 'insanity', a symptom or complication not hitherto described by any writer on kala-azar, for about a fortnight before she came for hospital treatment. It is remarkable that the mental condition of the girl became normal after 4 injections. She gained 21 pounds in weight after treatment.

* Being a paper read at the Annual General Meeting of the Surma Valley and Chittagong Division of the British Medical Association held at the Lungla Club on 26th January, 1946.

† The paper condensed by the editor.

Two cases—20 and 21—had 13 and 15 injections respectively of urea stibamine without any effect and have, as such, been termed urea stibamine resistant cases.

Dosage.—The dosage originally recommended by the makers was a total of 60 c.cm. in 10 to 21 days, (i) 2 c.cm. on the first, 4 c.cm. on the 3rd and then 9 injections of 6 c.cm. each on alternate days, or (ii) 10 injections of 6 c.cm. daily or on alternate days. As the drug produced no untoward reactions, the dose was gradually increased and a single dose of 10, 15 or even 20 c.cm. was well tolerated. Subsequently the makers recommended a total maximum dosage of 200 c.cm. The usual dosage followed in the treatment of these 25 cases was 10 c.cm. on alternate days up to a maximum of 200 c.cm. for an adult weighing about 8 stones.

Reactions.—The drug produced no untoward reactions irrespective of the routes of administration.

Contra-indications.—Nephritis and ascites are contra-indications as stated by the makers. But both these conditions are not uncommonly associated with kala-azar. The writer successfully treated a few patients with the above conditions after the administration of strong alkaline diuretics by mouth which relieved both ascites and albuminuria.

Results of treatment: (1) *General.*—With each injection the patients looked brighter and experienced a feeling of well-being.

(2) *Fever.*—In most cases the fever dropped to normal and remained at that level after 2 to 4 injections. As kala-azar patients usually run intermittent temperature, those cases in which the treatment was commenced during the afebrile phase never showed a rise above normal again (except a transient rise for any superimposed infection).

(3) *Hæmoglobin.*—There was an appreciable increase in hæmoglobin percentage in all but 2 cases. The lowest hæmoglobin was 45 per cent, the highest 75 per cent and the average 61 per cent against 30 per cent, 55 per cent and 43 per cent respectively before treatment. Even case 25 which was not cured had an increase of 20 per cent in hæmoglobin probably due to the effect of hæmatinics.

(4) *Leucocytes.*—There was a distinct increase in leucocyte counts in all the cases after treatment. The average count was approximately 6,500 per c.mm. against 3,000 per c.mm. before treatment.

(5) *Spleen.*—There was a rapid and remarkable diminution in the size of the spleen in all cases except one (case 25), and at the same time it became softer. The protocol will show that some spleens previously measuring 6 to 7 inches were not even palpable after treatment.

(6) *Weight.*—Each case gained weight after treatment. One gained as much as 21 pounds, the minimum weight gained was 2 pounds but the great majority gained 4 to 14 pounds.

(7) *Aldehyde reaction.*—This was negative in all but 2 cases (16 and 25) after treatment. Case 16 had a negative final urea stibamine test and spleen puncture. Case 25 was a failure of treatment.

(8) The final urea stibamine reaction was negative in all but case 25.

(9) Final spleen puncture smear was negative in all the 3 cases in which it was done. The size of the spleen in other cases did not permit a puncture.

(10) Final sternal puncture smear was positive in only one (case 25) out of the 4 cases done. The clinical, the hæmatological and other responses were so very decisive of an immediate cure that the complicated process of sternal puncture to which the patients agreed with some reluctance was not thought essential for establishing a cure in each case.

Discussion.—It will appear from the above that 24 out of 25 cases treated with stibatin fulfilled the following criteria of immediate cure: (i) Sense of well-being. (ii) Return of temperature to normal and maintenance at that level. (iii) Increase in hæmoglobin percentage. (iv) Increase in white cell counts. (v) Increase in weight. (vi) Marked reduction in size of the spleen. (vii) Negative aldehyde and urea stibamine reactions. So the immediate cure rate was 96 per cent. Napier has emphasized (Napier and Sen Gupta, 1943) 'Parasitological evidence is no more reliable than clinical and time alone can indicate if an apparent cure is a complete cure. It may be said that if a patient relapses, he does so within 6 months after a course of treatment.' Twenty-three out of the 25 cases treated with stibatin were regularly followed up and 22 of them (except case 25 who is being treated with urea stibamine) were found well and without symptoms at the end of 6 months. Case 9 could not be followed up as he was repatriated to his home district shortly after the completion of the treatment and case 23 unfortunately died of cerebral malaria on 27th July, 1944, within about 19 weeks of the completion of the course but he was free from symptoms all these weeks. Leaving out these two cases 22 out of 23 or 95.65 per cent of the cases had permanent cure. Assuming that the two cases which could not be followed up were failures, the permanent cure rate was 88 per cent.

Comparison and conclusions.—In our armamentarium against kala-azar we have two classes of compounds: (i) the pentavalent antimony compounds, like neo-stibosan and urea stibamine, to which this new pentavalent antimony compound 'stibatin' may be added, and (ii) the diamidine compounds like diamidino-diphenoxy-pentane and diamidino-stilbene. The latter two non-antimonial compounds have been found unsuitable for mass administration for their toxic reactions and neuropathic sequelæ, and pentavalent antimony compounds

Serial number ..	1	2	3	4	5	6	7	8	9	10	11
Age in years ..	35	30	12	15	12	50	35	45	12	40	50
Sex ..	M.	M.	M.	M.	F.	M.	F.	M.	M.	M.	M.
Duration of illness in months.	6	18	3	12	8	10	18	12	4	14	16
Hæmoglobin by Tallqvist's scale, per cent.	35	30	45	45	50	45	45	55	50	40	40
Leucocytes per c.mm. in thousands.	1.7	1.5	2.4	2.3	3.2	2.3	2.4	3.7	3.4	2.5	2.4
Weight in pounds ..	112	100	60	85	43	77	99	98	54	112	94
Spleen in inches below costal margin.	5	2.5	1	6	2	4	5	7	3	5	4
Aldehyde reactions ..	+++	++	++	+++	++	++	+++	+++	++	++	++
Urea stibamine test ..	+	+	+	+	+	+	+	+	+	+	+
Spleen puncture or sternum puncture.	SP +	ST +	ST +	SP +	ST +	SP +	SP +	SP +	SP +	SP +	SP +
Total dose of stibatin in c.cm.	130	150	85	223	105	180	200	170	70	152	151
Number of doses ..	15	15	16	22	21	18	20	17	14	20	20
Final hæmoglobin by Tallqvist's scale, per cent.	60	65	60	55	60	55	45	65	65	70	50
Final leucocyte count per c.mm. in thousands.	6.0	7.2	6.2	3.8	6.5	4.5	3.8	7.5	7.4	5.2	3.3
Final weight in pounds	117	104	65	89	64	79	105	107	59	127.5	102.5
Final spleen in inches below costal margin.	0	0	0	2	0	3	2	1	0	0	1
Final aldehyde test ..	—	—	—	—	—	—	—	—	—	—	—
Final urea stibamine test ..	—	—	—	—	—	—	—	—	—	—	—
Final spleen and sternal punctures.	ST—	..	SP—	ST—	ST—
Immediate result ..	C	C	C	C	C	C	C	C	C	C	C
Subsequent history ..	C	C	C	C	C	C	C	C	RP	C	C

UR = Urea stibamine resistant case; SP = Spleen home; CM = Cerebral malaria; JP = Just palpable;

have been advocated as the best anti-kala-azar drugs at our disposal now. The above records show that—(1) Stibatin or sodium antimony gluconate possesses definite anti-kala-azar activities. (2) Its permanent cure rate (95.65 per cent) is higher than that of the best recognized antimonial anti-kala-azar compound neo-stibosan (91.28 per cent, Napier, Sen Gupta and Sen, 1942) and also than that of diamidino-stilbene (94.29 per cent, Napier, Sen Gupta and Sen, 1942). (3) Stibatin is practically non-toxic. (4) Its advantages over urea stibamine, diamidino-diphenoxy-pentane and diamidino-stilbene are that it can be administered both intramuscularly and intravenously without any risk and that it is far less toxic than any of the latter drugs. (5) It is suitable for treating children and corpulent patients and patients with general anasarca. (6) It is effective in urea stibamine resistant cases. (7) It is not expensive. So it deserves trial in more extensive fields.

Acknowledgment

The writer is highly thankful to Dr. E. Burke, late of Mangaldai Medical Association, Darrang, Assam, for introducing the product to the writer, and to Messrs. H. J. Foster and Co., Ltd., Bombay, for their supplying stibatin free for clinical trial.

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ACTIVATION OF THE HUMAN SYSTEM IN FILARIASIS

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The usual opinion: depression caused by filariasis

THAT depression occurs in chyluria caused by filariasis has been known for some time (Manson and Shipley, 1907; Manson-Bahr, 1940; Strong, 1942).

Lately attention has been drawn to a depression caused by filariasis generally although

OL

12	13	14	15	16	17	18	19	20 UR	21 UR	22	23	24	25
10 M. 15	38 M. 18	40 M. 9	45 F. 24	48 M. 20	12 M. 6	16 M. 8	12 F. 12	12 M. 6	40 M. 20	45 M. 12	16 M. 14	10 F. 8	40 M. 24
35	55	45	45	45	35	55	45	45	30	35	40	40	40
3.4	3.6	3.0	2.8	3.0	1.8	3.8	2.4	2.8	1.6	1.8	2.5	2.6	2.5
70 6	100 3	85 6	95 7	85 7	61 4.5	85 4	59 6	56 1.5	100 4	89 5	84 4	85 3.5	100 4
+++ + SP +	++ + SP +	+++ + SP +	+++ + SP +	+++ + SP +	++ + SP +	++ + SP +	+++ + SP +	++ + ST +	++ + SP +	+++ + SP +	++ + SP +	++ + SP +	+++ + SP +
66	62	162	60	60	35	60	30	105	180	180	160	64	180
23 50	11 55	17 60	11 60	11 55	13 70	11 65	11 60	18 70	23 70	23 50	23 75	14 70	19 60
5.2	6.2	5.8	7.0	4.8	7.5	6.0	6.5	8.0	5.0	4.8	7.0	8.5	6.5
75 0	106.5 1	91.5 0	103 0	95 3	80.5 1.5	91.5 1	65 2	68 JP	109.5 1.5	105 1	96 3	99 2	115 4
—	—	—	—	+	—	—	—	—	—	—	—	—	+
—	—	—	—	—	—	—	—	—	—	—	—	—	+
..	SP —	SP —	..	ST +
C	C	C	C	C	C	C	C	C	C	C	C	C	Not cured.
C	C	C	C	C	C	C	C	C	C	C	Died of CM.	C	Not cured.

puncture; ST = Sternal puncture; RP = Repatriated
C = Cured.

racial exceptions have been made. 'Many observers have noticed the mood disturbance associated with the acute phases of tropical parasitic infestations. Particularly is this true of filariasis. As with all systemic infections, there are fatigue, irritability, mild depression and anxiety. However, in addition there is a pervading element of apprehension and concern in the case of white troops which is absent in the infested native population' (Rome and Fogel, 1943).

Again, 'profound psychological changes are found in filariasis specially when these occur in American soldiers' (Editorial, 1944).

Present writers' opinion : activation caused by filariasis

The present writers believe that filariasis unless crippling or disabling sexually because of marked elephantiasis is productive of mental and sexual activation. They have on their register: (1) Europeans in business who have risen to be merchant princes, after resenting spending a shilling on haircut, on their first voyage out, instead of eight pence they paid at home. They are known to enjoy life in their sixties in a way which most men in their thirties envy. (2) European widows who have

remarried after unusually long periods of freedom in which they have developed filariasis. (3) Indian businessmen who have revived failing business more than once. (4) Young publicly-minded Indians who, in spite of holding extreme views, stand head and shoulders above others in placing social reform before political advancement. (5) Indian officials in provincial service who have risen high from initially modest levels. (6) Indian medical men who hold optimistic views on pessimistic problems, are well abreast of recent advances and doing well too. A few examples are given in the table appended.

Two observations on two endemic areas in India provide further evidence in the same direction: (1) In Orissa is situated the famous temple devoted to sexual matters. (2) Malabar has a very high fertility rate and an equally high literacy rate.

Does the adult worm function as a gonadal implantation?

An optimistic prognosis for future sufferers

The fact that the erysipeloid attacks leading to elephantiasis can be controlled so quickly with sulphonamides should banish all pessimism. Future sufferers should be quite as optimistic in getting over filariasis as in getting

TABLE
Some filariasis cases specially observed during 1943-45

Register No.	Patient's name	Age	Race	Sex	Occupation and locality	Disease	Duration in years	Laboratory findings	REMARKS
215/43	S. J.	58	A-I.	F.	Representative, Salvation Army, Cal.	Filarial lymphangitis, both legs.	20	Mf. -, Eosin. 7 per cent	Very active for the age.
351/43	F. S. L.	60	E.	M.	General Manager, Typewriter Co., Cal.	Filarial lymphangitis, L. leg.	12	Mf. -, Eosin. 7 per cent	Successful businessman with advanced views.
550/43	S. R.	50	E.	F.	Business, Cal.	Filarial lymphangitis, L. leg.	8	Mf. -, Eosin. 5 per cent	Very active for the age.
790/43	C.	26	Indian, H.	M.	Journalist, Benares Service, Cal.	Chyluria	7	Mf. +, Eosin. 10 per cent	Of advanced views.
34/44	S. N. D. D.	30	"	M.	Service, Cal.	Lymphangitis, R. arm	2	Mf. +, Eosin. 12 per cent	Successful in service, rapid promotions.
64/44	S. M.	54	"	M.	Business, Cal.	" scrotum	26	Mf. -, Eosin. 3 per cent	Exceptional success in business.
221/44	R. B.	40	"	M.	Service, Cal.	"	9	Mf. -, Eosin. 10 per cent	Rapid rise in office.
292/44	W. V. K.	40	A-I.	M.	Engineer, Cal.	R. leg	5	Mf. +, Eosin. 9 per cent	Exceptional success in service.
295/44	R. R.	40	Indian, H.	M.	Accountant, Cal.	Ep-orchitis bil.	12	Mf. +, Eosin. 4 per cent	Rapid rise and success in service.
410/44	N. M. M.	45	Parsee	M.	Manager, Insee. Co., Cal.	Lymphangitis, scrotum	20	Mf. -, Eosin. 12 per cent	Reached top in office.
423/44	V. S.	45	Indian, H.	M.	Accounts Officer, Cal.	" R. leg	8	Mf. -, Eosin. 14 per cent	Promoted to officer's rank.
456/44	Z.	60	Indian, M.	M.	Merchant, Cal.	Chyluria	15	Mf. +, Eosin. 6 per cent	Merchant prince.
485/44	M. S. R.	40	Indian, H.	M.	Engineer, Cal.	Lymphangitis, R. arm	10	Mf. +, Eosin. 14 per cent	Of advanced views.
513/44	I. J.	52	I. Ch.	M.	Medical man in Research Dept., Cal.	" L. leg	20	Mf. -, Eosin. 5 per cent	" " "
599/44	C. W. B.	57	E.	M.	Colliery Manager, Manbhurn.	Elephantiasis, L. leg	25	Mf. -, Eosin. 4 per cent	Rapid promotion.
5/45	B. M. P.	50	Indian, H.	M.	Merchant, Buxar	Lymphangitis, scrotum	10	Mf. -, Eosin. 13 per cent	Successful businessman.
67/45	R. K.	50	"	M.	Officer, Mercantile Office.	Ep-orchitis, L.	12	Mf. +, Eosin. 8 per cent	Exceptional promotion in service.
74/45	R. K. D.	42	"	M.	Businessman, Cal.	Lymphangitis, leg and scrotum.	10	Mf. +, Eosin. 10 per cent	Successful businessman.
96/45	T.	40	"	M.	"	Elephantiasis, scrotum	10	Mf. -, Eosin. 11 per cent	Exceptional success in business.
128/45	S. J. S.	60	Parsee	M.	Lawyer, Allahabad	Ep-orchitis	20	Mf. -, Eosin. 8 per cent	Successful in profession.
140/45	S.	29	Jew	M.	Business, Cal.	" L. leg	2	Mf. +, Eosin. 12 per cent	Exceptional success in business.
186/45	B. T.	35	Indian, H.	M.	Technician, Cal.	Lymphangitis, scrotum	5	Mf. +, Eosin. 11 per cent	Rapid promotions.
188/45	V. S.	42	"	M.	Accounts Officer, Cal.	"	12	Mf. +, Eosin. 6 per cent	Exceptional success in service.

Abbreviations: A-I. = Anglo-Indian; E. = European; Indian, H. = Indian, Hindu; Indian, M. = Indian, Muslim; I. Ch. = Indian Christian; Ep-orchitis bil. = Epididymo-orchitis, bilateral; Cal. = Calcutta; Mf. = Microfilariae; Eosin. = Eosinophiles; R. = right; L. = left.

over malaria. Further, their medical advisers should know that both the conditions may not be unmixed evils.

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OBSERVATIONS ON 'EOSINOPHILIC LUNG'*

By K. U. JHATAKIA, M.D.

A good deal of interest has been created since the publication of the paper by Frimodt-Møller and Barton in 1940, and during the last few years many papers have been published on this interesting syndrome. Chief contributions have come from Weingarten (1943), Treu (1943, 1944), Simeons (1943), Owen (1943), Heilig and Visweswar (1943), Vaidya (1943), Patel (1943, 1944, 1945), Parsons-Smith (1944), Chaudhuri (1943), Chakravarty and Roy (1943), Emerson (1944), Leishman and Kelsall (1944), Carter, Wedd and D'Abrera (1944), Soysa and Jayawardena (1945) and a few more.

During the year 1945, 140 cases were encountered by the writer. The cases in this series have been collected chiefly from the J. J. Hospital, Sir Hurkisandas Hospital and Devkaran Muljee Pathology Laboratory. The approach has been either direct or indirect. 'Direct' means where the patient consulted the doctor for some symptom of this syndrome, while 'indirect' approach means where the patient came to the laboratory for routine blood examinations, with some other diagnosis from outside but the blood picture was suggestive of this syndrome. The patients in the latter group were then examined for the presence of symptoms and signs of this condition.

The following criteria were considered in deciding a case as one of eosinophilic lung: (1) History of asthmatic attacks, chronic cough and/or some of the symptoms of this syndrome described later. (2) A total white cell count more than 10,000 per c.mm. and eosinophil count more than 15 per cent. (3) Exclusion of other conditions causing eosinophilia. My

observations on various aspects of this syndrome in the present series of cases are grouped under the following headings—ætiological, clinical, laboratory, radiological, and therapeutic.

Ætiological aspects.—(a) *Locality and climate.* All the cases were persons staying in Bombay. I think a damp climate acts as a predisposing factor. Most of the chronic cases complained that the symptoms aggravated during the winter.

(b) *Caste and community.* The condition is seen in all communities, even in foreigners visiting India. Out of 140 cases there were 123 Hindus, 15 Mohammedans, 1 Parsee and 1 Christian. These figures, however, cannot be taken as representative because of the type and locality of the hospitals, and the nature of the practice.

(c) *Occupation.* This does not appear to have much importance, but two cases (in females) are worth mentioning. They were quite well till food rationing was introduced. The trouble began when they started cleaning the ration food-grains. This history is similar to the one obtained by the Ceylon workers in cases of this type where inhalation of the dust from grain stores, etc., was the chief exciting factor in starting the trouble. Both these cases responded well to arsenic treatment and became free from symptoms. The incidence of occupation in this series is given in table I.

TABLE I

Occupation	Number of cases
Domestic workers ..	24
Clerical workers and businessmen ..	26
Grainshop workers ..	39
Students, teachers and doctors ..	12
Industrial workers ..	18
Miscellaneous ..	21
TOTAL ..	140

(d) *Sex.* There were 98 adult males and 8 male children (total 106 or 75 per cent); 30 adult females and 4 female children (total 34 or 24 per cent).

TABLE II

Age group	Number of cases	Percentage
1 to 10 years ..	12	9.4
11 to 20 " ..	30	21.0
21 to 30 " ..	65	46.0
31 to 40 " ..	25	18.0
41 to 50 " ..	6	4.2
51 to 60 " ..	1	0.7
61 and above ..	1	0.7

(e) *Age.* The age incidence in the present series of cases is given in table II.

* Abridged from a paper read at the staff meeting of Sir J. J. group of hospitals and Grant Medical College, Bombay, on the 7th February, 1946.

The youngest patient was one year and the oldest 62 years old.

(f) *History of allergic diathesis in the family.* Weingarten found no such history in his cases, while Patel observed that such history could be obtained in his. In my series there were 12 cases with definite history of allergic manifestation in some of the family members. I have come across six families where there were more than one member suffering from this syndrome.

(g) *Duration of illness.* This varied from a few weeks to some years, as shown in table III.

TABLE III
Duration of present complaints

	Cases
0 to 1 year ..	106
1 to 5 years ..	31
5 to 10 " ..	2
10 to 15 " ..	1
TOTAL ..	140

The shortest period was 16 days and the longest 15 years. In the majority of patients the duration was between 3 and 8 months.

Clinical aspects.—The clinical features are very variable, and the only constant feature is leucocytosis with high eosinophilic count, which dramatically responds to organic arsenicals. In most cases the mode of onset is gradual. The patient gets a cough which is at first neglected. It persists and may be followed later on by a sense of choking in throat, heaviness in chest and feeling of suffocation. This chain of symptoms is completed by precipitation of breathlessness or asthmatic attack. This is the picture observed in the majority of cases. Cough is usually dry, hacking and unproductive. It comes in a paroxysm and is more marked at night. Frequency of paroxysms increases till the patient gets an asthmatic attack. The interval between the onset of cough and the dyspnoea varied from a few weeks to a few years. During this interval the patient may complain of a sense of fatigue and loss of weight, appetite and energy. In 28 of my cases patients complained of cough only and never got dyspnoea at any time. Some patients ran a low, irregular and intermittent temperature along with these features. The symptoms may be aggravated by exposure to cold. In one group acute asthmatic attacks dominate the picture and in another group the syndrome gradually proceeds to chronic stage not yielding to sedative expectorant mixtures or anti-asthmatic drugs, and may go on for years. In the acute stage, the patient sometimes runs a high temperature which might be

continuous or intermittent and may last a few weeks or even months. Blood examination at this stage is very helpful for correct diagnosis.

Physical examination shows signs of mild bronchitis. Hyper-resonance of the chest and prolonged expiration are constant features in most cases. One feature worth mentioning is that even in the acute asthmatic the rhonchi are much less than in acute bronchial asthma. In chronic cases, occasional crepitations at bases are met with. Hæmoptysis has been reported in a few cases (Viswanathan, 1945). Splenic enlargement is reported by Weingarten (1943) and Simeons (1943), but Patel (1943, 1944, 1945), Misra (1945) and others were unable to find it; it was present in only three cases in my series. Patel noticed enlargement of the lymph glands in about 45 per cent of cases but I could find only in two.

The chief clinical findings are given in table IV.

TABLE IV
Clinical findings

	Cases
Cough	112
Asthmatic attacks	102
Loss of weight and appetite	19
Prostration, loss of energy, fatigue ..	29
Choking, sense of suffocation and discomfort in chest.	42
Fever	16
Lung signs	81
Hæmoptysis	1

From table IV it is clear that cough and breathlessness are the most important findings. All features are not always present in all the cases and frequently a patient comes for only one presenting feature and others may be detected on examination only. The chief presenting symptoms vary and if this is not kept in mind the diagnosis may be missed. Some patients come with vague symptomatology, while others with any combination of the above features. Cases were, however, met with where the presenting symptoms were quite different as exhibited by the following cases:—

Case 1.—A doctor brought his wife's blood for examination, as she complained of prostration and exhaustion. There was no other complaint. The blood showed a white cell count of 18,650 with 51 per cent eosinophils. She was given a course of acetylsalicylic acid injections after which the blood count returned to normal and she was much improved. The sense of exhaustion and fatigue completely disappeared.

After this incident I watched for this symptom among my outpatients and I got two similar cases. In one there was history of dry cough for a short time. Both turned out to be cases of this syndrome on blood examination and were completely relieved on treatment.

Case 2.—A female, aged 38 years, complained of attacks of vague precordial pain, not related to any particular factor and unaccompanied by any sweating, palpitation, cough or dyspnoea. She tried many drugs from various doctors but all in vain. Blood pressure and x-ray findings were normal. Kahn test was negative.

Electrocardiogram was normal. As her symptoms increased, she came to Bombay. Her blood count showed white cells 42,500 per c.mm. with eosinophils 45 per cent. She was given a course of acetylsarsan and the symptoms disappeared.

Case 3.—A young man, aged 23 years, was admitted to the Hukisandas Hospital for irregular fever off and on for about 10 months. The temperature used to range between 99 and 101°F. At the beginning he was seen by a doctor at Madras and was provisionally labelled as tuberculosis because he had cough, loss of appetite, night sweats and mottlings in the skiagram.

During hospital stay he was running a temperature between 99 and 101°F. He had a dry cough but no asthmatic attack. He had lost about 27 pounds in weight in 10 months. The only positive findings were the presence of a few crepitations in both the bases and a soft systolic murmur at the mitral area conducted to axillary space. The patient gave a history of joint pains 10 years ago. The skiagram of the chest showed diffused mottling in both lungs, more marked at the hilar area. There was no splenic enlargement. Sputum was repeatedly negative for tubercle bacilli. The blood examination, on admission, showed 10,400 white blood cells with lymphocytes 30 per cent, large mononuclears 3 per cent, polymorphonuclears 60 per cent and eosinophils 7 per cent.

For about three months the patient had an irregular temperature. Widal was negative twice and other agglutination tests were also negative. Because of the murmur and fever, the possibility of subacute bacterial endocarditis was thought of, but the blood culture was repeatedly negative.

Blood was then re-examined and it showed 63,450 white cells per c.mm. with lymphocytes 15 per cent, polymorphonuclears 12 per cent, and eosinophils 73 per cent. Other causes for such a count were excluded. The patient was then given a course of 10 injections of acetylsarsan with complete recovery in a month. Prior to acetylsarsan he was given liver extract, vitamin B injections, sulphonamides, calcium, cod-liver oil, yeast, nicotinic acid and blood transfusions, but none had any effect on his fever or other symptoms. After the first acetylsarsan injection he had a flare-up next day, which subsided on the third day. After five acetylsarsan injections the temperature was normal and the white cell count was 10,120 per c.mm. with eosinophils 29 per cent. Five more injections were given and the blood count a few days before discharge was 8,240 white cells per c.mm. and eosinophils 13 per cent.

These case reports show how the clinical picture may vary from simple exhaustion and fatigue to prolonged irregular pyrexia for 10 months. Considering these clinical features I think these cases can be grouped under three types :

(1) Ambulatory type, where the symptoms are vague as described in case 1 and diagnosis is made only on blood examination.

(2) Acute type, where the symptoms are typical and of short duration and acute in nature. The patient has cough and/or asthma associated with or without fever.

(3) Chronic type, where cough with or without history of asthmatic attack is present for more than a year.

Other points worth noting along with the clinical picture are : (1) Can tuberculosis be associated with this syndrome? It was at first considered unlikely, but later Treu, Shah and others have reported its presence along with tuberculosis. I had none in this series. (2) Do these patients get spontaneous relief? Patel has reported the possibility of temporary spontaneous relief. Patients often come with

history of similar complaints previously and so it is quite possible that they get spontaneous relief following first attacks. Relapses have been known even after thorough treatment.

Laboratory findings.—(a) *Blood examination.* This was done in all cases and repeated in some. In all it showed massive eosinophilia with leucocytosis. The white cell count varied from 10,150 to 81,500 per c.mm. The eosinophil percentage varied from 15 to 90. It has been observed that the percentage does not increase always proportionately to the increase in the total white cell count. A higher rate was met with in cases with white cell counts below 30,000 per c.mm. while a lower rate was often obtained with white cell counts above 30,000 per c.mm.

TABLE V
Absolute eosinophil counts

Absolute eosinophil count in hundreds	Number of cases	Approximate percentage
15 to 25	16	11.0
26 to 50	15	10.5
51 to 100	51	37.0
101 to 150	24	17.0
151 to 200	14	10.0
201 to 250	8	5.7
251 to 300	6	4.3
301 to 350	2	1.4
351 to 400	1	0.7
401 to 500	1	0.7
501 to 600	1	0.7
601 to 700	1	0.7

The severity of symptoms are not related in any way with the blood count. Maximum distress was observed in a patient with 12,000 white cell counts and 18 per cent eosinophils, while the symptoms were very mild in spite of a blood picture showing 52,400 white cells per c.mm. with 56 per cent eosinophils.

(b) *Sputum examination.* Presence of mites in the sputum of 17 out of 28 cases has been reported by Carter, Wedd and D'Abrera (1944). The method suggested by them is time-taking and laborious. I have been able to do this only in 4 cases. In one we could find only one mite after a long search, while in the rest nothing was detected. Routine sputum examination for tubercle bacilli and other organisms was done in 21 cases only, but nothing in particular was reported. Charcot-Leyden crystals and Curshman's spirals were not so frequent as in allergic asthma. Special examination for spirochaetes under dark-ground illumination could be done in a few cases only and it was negative in all.

(c) *Stool examination.* Routine stool examination in 17 cases showed cysts of *E. coli* in 2, ova of ankylostoma in 1, ova of roundworm in 1, and cysts of *E. histolytica* in 2; in the rest there was nothing in particular.

Routine examination of urine in 24 cases, urine culture in one case of prolonged pyrexia,

blood culture in one case, and blood chemistry in two cases all revealed normal findings. Erythrocyte sedimentation rate done in two cases showed a moderate increase.

Sternal punctures were performed in 7 cases by Patel and in 6 cases by Viswanathan. Nothing abnormal except eosinophilic myeloid reaction was reported. Lymph gland biopsy was done in Patel's cases and the histological findings reported were subacute lymphadenitis; eosinophilic infiltration was not seen. Animal inoculations with citrated blood were performed in a few cases of Patel but with negative results. Cold agglutination test was performed in a series of 61 and 85 cases of this syndrome by Viswanathan and Natarajan (1945) and consistently high titre values have been obtained in 90 per cent of their series. Gupta (1945) found positive W.R. but negative Kahn in some cases of this syndrome in the absence of any history of other signs of syphilis.

Radiological findings.—The typical x-ray picture shows symmetrically distributed 'shadows' on both sides, suggesting a bronchogenic dissemination. Numerous discrete shadows, scattered throughout the lungs, produce a typical mottling appearance. The skiagram is always better than screening in these cases. The following observations are worth noting :

(a) Shadows are more marked in the early than in the chronic cases.

(b) No shadows were detected in the ambulatory type of cases.

(c) The extent of lung shadows was not proportionate to the severity of symptoms and *vice versa*.

(d) The shadows could not be correlated with the total white cell and eosinophil counts.

(e) The shadows disappeared or became much less prominent with treatment. Spontaneous disappearance of shadows have not been reported yet.

(f) Pulmonary shadows are not present in all cases. In this series out of 52 patients screened, mottling was reported in 32 only. Twenty-four of them were of acute type, and 8 of chronic type.

Therapeutic findings.—Frimodt-Möller and Barton (1940) reported 175 cases which were observed between 1925 and 1940, but no suggestion of treatment came till Weingarten reported in 1943 arsenic as curative in this syndrome. Treu in 1944 mentioned that this was known to him since 1933. I have known many doctors who have made names as 'asthma specialists' by using arsenic much earlier than 1933, and in all probability many of their asthma cases belonged to this syndrome.

Various preparations of arsenic are used but with the same results. Most of my cases were treated with 6 to 8 injections of acetylarsan by the intramuscular route. It was given every fourth day in 3 c.c.m. doses. Arsenic by oral route is also reported to be useful. The pre-

parations used are carbarsone, stovarsone or leucarsone which contain about 27 to 28 per cent of arsenic. A 4-grain tablet is given twice a day for 10 days and the same course is repeated after one week's interval. Good effect has been observed by all writers with arsenic by whatever route it is given. I have observed the following in connection with this form of treatment.

(a) There was a flare-up after the first or second injection in 9. All of them were of acute type. The symptoms became aggravated and the blood count showed a tendency to rise. These features persisted for a few days and then subsided gradually with or without further treatment. In one case where carbarsone was given by mouth in usual dosage, the patient's white cell count rose from 15,000 to 33,500 per c.mm. and the eosinophils from 43 to 78 per cent at the end of 10 days' treatment. His symptoms increased in severity and he started having acute attacks of asthma. I then changed to acetylarsan and he felt much better after 2 injections. The white cell count came down to 10,200 per c.mm. and the eosinophils to 8 per cent after six injections when the patient became symptom free. This phenomenon looks like Herxheimer's reaction.

(b) The relief rate differs in individual patients and could not be correlated with the severity of symptoms, blood count or arsenical preparation used. Some patients with severe symptoms felt much better after one injection while others with milder symptoms took longer time in getting relief. The same thing was observed as far as blood count was concerned, and patients often got relief from symptoms even before the blood count returned to normal.

(c) The rate of return of blood count to normal level varies much irrespective of drugs used, or the height of blood count. It takes 6 to 10 weeks before it is normal.

(d) Some failures and relapses have recently been reported.

Diagnosis.—Diagnosis is made from the clinical picture and a typical blood count. X-ray findings may help in final confirmation. One point, I want to emphasize, is that fluctuations in blood counts may be observed and so it is necessary to repeat the blood examination after an interval, if one clinically suspects this syndrome. I met with two such cases. In the first the white cells were 23,240 per c.mm. and eosinophils 36 per cent, and in the second 18,560 per c.mm. and 24 per cent respectively. They were advised to have a course of arsenic but they did not take it for some reason or other. They came to me later and said that they were feeling much better with some cough mixture; the white cells were found to be 9,560 and 8,840 per c.mm. and the eosinophils 14 and 15 per cent respectively. After about 3 to 4 weeks, one of them got an acute attack of breathlessness and the other got severe paroxysms of cough and the blood counts were

24,560 with 42 per cent eosinophils, and 21,220 with 36 per cent eosinophils. They now consented to take acetylarsan and got cured after it.

Although there are many conditions which may give rise more or less to one or other features of eosinophilic lung, the diseases with which it is most likely to be confused are bronchial asthma, parasitic infection, certain skin, blood and allergic conditions, and tuberculosis, but the diagnosis is not difficult if the clinical features and the results of blood and x-ray examinations are correlated together.

Discussion.—Many suggestions have been put forward about the ætiology of this syndrome and these may be briefly referred to here.

(a) *Histamine theory.* Alexander (1941) described a type of asthma which he named 'intrinsic asthma' which is different from the usual allergic type because of its chronicity, remissions, absence of allergic history, and presence of high white cell and eosinophil counts. He attributed the cause to a histamine-like substance. This 'intrinsic asthma' is very much like the eosinophilic lung syndrome and in all probability it might be the same, but nobody has yet produced any evidence of such chemicals circulating in the body in such cases.

(b) *Allergic.* Frimodt-Møller and Barton (1940) and Weingarten (1943) postulated an allergic basis, because of asthmatic features and eosinophilia. This is open to objection, because in other allergic conditions, one rarely gets so high a white cell count and general constitutional features such as fever, prostration, lymphadenopathy, splenomegaly, etc. Secondly, there is a good response to antispasmodics, vasodilators, iodides, opiates, adrenalin, calcium, etc., in allergic conditions but not in this syndrome. It is also difficult to understand why arsenic should act specifically in this condition.

(c) *Parasitic.* Carter, Wedd and D'Abbrera (1944) reported presence of mites in the sputum of such cases. It is difficult to understand how these mites produce fever, loss of appetite, leucocytosis, eosinophilia, etc.

(d) *Virus.* Can this be a virus infection? And is it not possible that those mites might be acting as vectors for them. Eosinophilia is observed in virus diseases like variola, scarlet fever, etc. Viswanathan and Natarajan (1945) have observed cold agglutination test positive in high titre in about 90 per cent cases of their series. Such titre values are also observed in primary atypical pneumonia which is probably of virus origin. Further work may be helpful to decide as we do not know whether cold agglutination test is also positive in other conditions, including allergic ones.

(e) *Spirochætal.* Can this be some spirochætal infection? All other features such as fever, glandular enlargement, cough and the specific effect of arsenic favour this. Leucocytosis up to 20,000 is often met with in secondary

syphilis and other spirochætal infections. Eosinophilia is also often met with in syphilis (Spangler, 1935), but the asthmatic attacks are difficult to explain. Detailed examination of sputum for spirochætes, etc., may be useful.

Summary.—(1) One hundred and forty cases of eosinophilic lung seen during the year 1945 are analysed.

(2) Available literature on the subject is reviewed.

(3) Ætiology of the syndrome is discussed and its incidence according to age, sex, occupation, etc., is described.

(4) Clinical findings are analysed and it is shown that though cough and asthma are the chief symptoms of this syndrome, some cases do show unusual features. A few atypical cases are described.

(5) Occurrence of the syndrome in more than one member in the family is reported.

(6) Findings on blood examination are fully described. Incidence of total white cell and eosinophil counts and eosinophil percentage is discussed. It has been shown that there is no correlation between the blood findings and clinical picture.

(7) Other laboratory investigations done in these cases are reported.

(8) Typical radiological findings are described. These were not positive in all cases, and there was no correlation of findings with either clinical or hæmatological picture.

(9) On the basis of findings the cases can be grouped as ambulatory, acute, and chronic types.

(10) Therapeutic effect of arsenic is uniform with oral as well as parenteral administration. Phenomena of flare-up are observed in a few cases during treatment. Failure of arsenic in a few industrial workers is reported.

(11) Diagnosis is discussed.

(12) Theories about the syndrome are discussed. The real cause still remains obscure.

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LEUKÆMOID REACTION AFTER BLOOD TRANSFUSION

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TRANSIENT leukæmoid reaction with its characteristic leucocyte picture showing a large number of immature myeloid cells in the peripheral blood may occur in exceptional instances, though very rarely. Below is reported a case showing this interesting hæmatological picture following blood transfusion. The patient was under our close observation during his 1½ years' illness.

Case report

A Hindu male, aged 45 years, an educationist by profession, had a previous history of duodenal ulcer from 1932-39. One of his molar teeth was extracted in November 1943, followed by persistent bleeding from the gums, stopping after 10 days of intensive treatment with hæmostatics. A month later he developed severe burning sensation in the chest and back rendering him very weak and anæmic. Intensive liver and vitamin therapy could not improve his general condition. The blood examination on 4th March, 1944, showed macrocytic anæmia as reproduced in the table. Next day a blood transfusion of 200 c.cm. was given, the donor being his eldest son. A severe reaction followed. The transfusion, however, improved the patient's condition considerably and bleeding from the gums stopped. For three months afterwards he continued to be all right.

In August 1944 his condition again deteriorated (as revealed by blood examination) and a blood transfusion was arranged. This time the donor was his second son. On 13th August 100 c.cm. blood was given. Blood examination after five days showed 54 per cent immature cells and the relation between immature and mature white cells was 54 : 46. No immature cells were detected during the previous examinations. The sternal puncture was done on 19th August, 1944, and the result is shown in the table. Myeloid-erythroblastic ratio was 49 : 1. Bone marrow was more

cellular as shown by the total nucleated cell count. The early cells of the myeloid series were present in increasing proportion in the marrow than in the peripheral blood.

Blood examinations were made on 16th December, 1944, 8th and 22nd January, 1945, and on the basis of these reports repeated blood transfusions were given of small quantities of blood varying from 100 to 150 c.cm. in amount and on not a single occasion the same type of leukæmoid reaction was found as was seen after the second blood transfusion in August 1944. The donor on the last two occasions was a group 'O' one.

After the last transfusion the patient started bleeding from his piles and a fissure in ano was also found. Operation under local anæsthesia was done. Bleeding could not be controlled and the patient died in June 1945.

Comments

Leukæmoid reaction has been observed in various conditions, viz (1) extreme sepsis, specially in children; (2) the bone marrow crisis of hæmolytic jaundice and sickle cell anæmia; (3) syphilis; (4) acute tuberculosis; (5) polycythemia vera; (6) erythroblastic anæmia of childhood, specially von Jacksch and Cooley types; (7) infectious mononucleosis; (8) pertussis; (9) mediastinal tumours; (10) osteosclerosis; (11) metastatic tumours in bone marrow, and (12) acute forms of Hodgkin's disease.

Feldman and Stasney (1937) have produced leukæmoid blood picture in tuberculous rabbits by injecting them with tuberculin. In most animals the total leucocyte count exceeded 100,000 cells per c.mm. with all types of immature myeloid cells.

The type of leukæmoid reaction after blood transfusion as observed in our case has not so far been reported. Another interesting feature is that it was not seen after other transfusion operations in the same patient. Blood matching was done both directly and indirectly on each occasion. The enlargement of spleen was not noted in this patient. The white cell count was too low to be of myelogenous leukæmia. Aleukæmic leukæmia cannot be considered, as immature white cells had not been detected before the blood transfusion and also in subsequent examinations.

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TABLE
Blood examination before and after repeated blood transfusions

Date	4-3-44	5-3-44	12-3-44	11-8-44	13-8-44	18-8-44	19-8-44	16-12-44	18-12-44	26-12-44	8-1-45	10-1-45	17-1-45	22-1-45	23-1-45	1-2-45
1. R.B.C. per c.mm. in millions.	2.03		3.5	1.2		1.98				4.1	3.5		4.0	3.2		4.2
2. Haemoglobin in gm. per 100 c.cm.	6.7		9.5	5.2		6.5				13	10.8		12.5	10.5		13.6
3. Packed cell volume, per cent.	25		36	18		22				44	40		42	35		45
4. Mean corpuscular volume, cu. μ .	123.1		102.3	150.0		111.1				107.3	114.3		105.0	109.4		107.1
5. Mean corpuscular haemoglobin, $\gamma\gamma$.	30.0		27.1	43.3		32.9				33.2	30.8		31.2	32.8		32.4
6. Mean corpuscular haemoglobin concentration, per cent.	26.8		26.4	28.9		29.5				30.9	27.0		29.9	30.0		30.2
7. W.B.C. per c.mm. ..	6,300		6,500	4,080		24,200	Nucleated cells per c.mm. 250,000	5,400		6,000	4,080		5,800	5,200		6,000
8. Differential white cells, per cent— (N. polymorphs E. do. B. do. Lymphocytes .. Monocytes .. Myeloblast .. Premyelocytes .. Myelocytes .. Metamyelocytes .. Immature .. Megaloblast .. Erythroblast .. Normoblast ..	62 1 Nil 36 1 Nil Nil Nil	I. Blood TRANSFUSION (200 c.cm.) Donor patient's eldest son. 68 2 Nil 28 2	68 2 Nil 28 2	60 0 Nil 39 1	II. Blood TRANSFUSION (100 c.cm.) Donor patient's second son. 34 Nil Nil 12 2 4 29 19	46 Nil Nil 12 2 4 29 19	4 28 22 18 23 98 1 1	60 2 Nil 35 3	III. Blood TRANSFUSION (60 c.cm.) Donor patient's second son. 65 2 Nil 32 1	62 1 Nil 34 3	64 1 Nil 33 2	59 2 Nil 36 3	V. Blood TRANSFUSION (150 c.cm.) Donor group 'O'. 63 2 Nil 32 3			
9. Immature red cells— Megaloblast .. Erythroblast .. Normoblast ..	Nil															

DIAGNOSIS OF INFECTIVE HEPATITIS IN ITS PRODROMAL AND INVASION STAGES

By MARIO STEFANINI, M.D. (Rome)

THE purpose of this short clinical note is to report some observations on the prodromal stage of infective hepatitis from a series of 28 cases lately seen in a military hospital.

Of unknown origin, infective hepatitis is a systemic disease with specific but not obligatory localization in the liver and possibly also in the small intestine, cæcum, mesenteric and cervical glands, pancreas, muscles, and nervous system. The infection takes place presumably through the nasopharyngeal and intestinal mucosa. The phase of penetration is followed by a stage of invasion and by another one, not always present, of localization in the liver.

The study of the prodromal stage of the disease has got not only diagnostic and prognostic importance but it may also suggest new ideas on the pathogenesis of the infection.

The following are the usual symptoms typical of the prodromal stage: dyspepsia, constipation, rarely diarrhoea, anorexia, nausea, and spasmodic cramp-like abdominal pains, sometimes of serious nature. These symptoms last for 6 or 7 days and then are still present when fever, which is considered the typical symptom of the invasion stage, sets in. The temperature is of remittent type, rapidly increasing in the initial period and often accompanied by chills and profuse sweating. Its final defervescence occurs by lysis, concurrently with the appearance of jaundice.

This sequence of symptoms is far more diagnostic than the type and duration of fever and the intensity and character of jaundice. Jaundice itself does not appear to be an obligatory symptom but it is most certainly a sign of seriousness of the disease as liver function tests show that icteric cases take much longer to recover than the non-icteric ones.

Acetonemic breathing and enlargement of the liver are also present in the initial stages. Out of my 28 cases, 19 (67.85 per cent) had also soft and tender spleens. The rapid distension of the liver is possibly a good explanation for the presence of a sharp pain on pressure at the right costo-vertebral angle.

I have also noticed in 22 of my cases (79.3 per cent) enlargement of posterior cervical glands which is probably an expression of the systemic infection that occurs in the disease. Especially diagnostic is the enlargement of a gland at the base of the neck just on the outer side of the sterno-mastoid muscle; hard, but not tender. This adenopathy disappears slowly in 5 to 6 days' time. In 5 cases (17.85 per cent) there has been generalized adenopathy.

Atypical cases sometimes make the diagnosis difficult in the prodromal and invasion stages.

Cases without fever or with high fever are particularly confusing.

Some pictures of the disease thought to be atypical ones, are really only expression of the behaviour of the infection, as for instance, the absence of hepatic localization will explain the non-icteric cases.

The laboratory tests are also of great help. Three to four days before the appearance of any symptoms, Franke's (1931) methylene blue test shows the presence of direct bilirubin in the urine. The test remains persistently positive for at least 15 to 25 days in non-complicated cases and becomes usually negative only a few days before the fading of jaundice. Flocculation tests appear strongly positive in the second or third day of dyspeptic troubles. I have followed Takata-Ara's test and Surgeon-General, American Army (1945), reports a similar behaviour with Hager's test. He also reports that bromsulphalein retention test and galactose tolerance test are usually positive at the beginning of the disease. Phosphatase activity of the serum is also very much increased. On the contrary, B.S.R., in my experience, remains normal during the infective and icteric stages at the end of which it markedly increases.

Present in the prodromal stage is also the typical blood picture of the disease: leucopenia with lymphocytosis and monocytosis, being about 20 per cent of the white cells, represented by young, immature lymphocytes.

The complex of clinical data reported above was in all cases sufficient for an early diagnosis of infective hepatitis which was later confirmed by the course of the disease and especially in the non-icteric cases, by the results of the laboratory investigations.

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GRANULOPENIA AND SULFA DRUGS

A CASE RECORD

By P. N. BARDHAN, M.R.C.P. (Edin.)

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THAT sulfa drugs can cause leucopenia, particularly granulopenia, is well known; it is usual to discontinue the drug if the granulocytes number less than 2,500 per c.mm. of blood; rarely the drug has been continued till the dangerously low level of 1,200 had been reached. Reports have not been seen where the drug has been administered in spite of an initial low leucocyte count. This short paper describes

just such a case where the initial leucocyte count was low and yet the sulfa drugs were urgently indicated.

Case notes

A lance-naik, aged 26 years, of an Indian State Infantry Battalion, was admitted into a military hospital, on the second day of illness, with cough, rusty sputum, pain in chest, all signs and symptoms of fever, dyspnoea, and severe anaemia. The diagnosis of lobar pneumonia was obvious and was also confirmed by physical examination. Treatment by sulfa drugs was of course indicated and would have been simple, but the severe anaemia gave warning of the usual leucopenia that generally accompanies severe anaemias.* The blood examination results showed: haemoglobin 2.9 grammes per cent, rbc 1.24 millions, and wbc 2,600 per c.mm. The differential count showed: granulocytes—neutrophil 63.0 per cent, eosinophil 0.5 per cent, basophil 0.0 per cent, monocytes 0.7 per cent and lymphocytes 36.5 per cent.

Polychromasia indicated that the bone marrow was capable of regeneration.

Other clinical features noted were haemic murmurs, and signs of avitaminosis, such as a sore and atrophied tongue, apathy, and a lustreless skin on the face.

The prognosis was serious and it was felt that death might occur from one or more of the following causes: (a) anoxaemia, (b) myocardial failure, (c) toxæmia, and (d) agranulocytosis.

(a) *Anoxaemia*.—A normal person can continue to live, if with difficulty, in an atmosphere of 12 per cent of oxygen. The patient having only 2.9 grammes per cent of haemoglobin, his oxygen carrying capacity was about 1/5 of normal, 14 to 15 grammes of haemoglobin being taken as normal. The normal atmosphere has 20 per cent of oxygen; the patient was therefore able to take 1/5 of 20 or 4 per cent only; but his breathing being at least twice as fast as the normal he would be taking in 8 per cent of oxygen in the same time period. There was just a chance therefore that he would continue to live for some time in spite of the relative anoxaemia. Further, it is known that in slowly developing anaemia the body can adapt itself to the low blood oxygen tension to a great degree. To make quite certain, however, the patient was given oxygen continuously for 48 hours by the intra-nasal catheter method. The rate of flow was so adjusted that the individual bubbles in the trap bottle could be seen but not counted. This ensured that the patient's rbc's would work at the maximum mechanical advantage and carry the maximum possible amount of oxygen.

(b) *Myocardial failure*.—Gross anaemia is often associated with fatty degeneration of the heart. But a heart that had apparently stood the strain of full regimental duties for months in spite of the anaemia would probably not be taxed much more because of the pneumonia. Rest in bed was of course obligatory, and was enjoined during convalescence also; mental rest was ensured by means of barbiturates.

* In case of acute infection in severe anaemia there may not be a leucopenia.

(c) *Toxaemia*.—Though young adults stand pneumonia well, the factor of anaemia made prognosis uncertain in this case. To combat the toxæmia, in addition to specific therapy, glucose was given by mouth and intravenously. Forty ounces of glucose in isotonic saline was infused by the drip method twice daily for 72 hours. Pulmonary cedema as a complication of this was a possible risk, but a carefully controlled drip and an adequate supply of oxygen were considered sufficient safeguards against this.

(d) *Agranulocytosis*.—This *per se* probably is not dangerous. It is the invasion by various organisms, against which the granulocytes are a first line of defence, that causes death. Reported cases of agranulocytosis following sulfa drugs show that the drug has to be given for about a week before there is any danger of granulopenia, leaving aside those cases which show an idiosyncrasy where the dosage is of no direct importance. The customary dosage of sulfa drugs, sulphapyridine in this case, needs at least 48 hours and generally 72 hours to produce clinically assessable results; this dosage does not ordinarily produce agranulocytosis, a risk that does not arise till the drug has been given for 5 or 6 days at least. It was felt that if the pneumococcal infection could be checked in 48 hours, agranulocytosis would not occur even if a large total dose of the drug was given within the period. The upper level of dosage of sulfa drugs is limited necessarily by the untoward side effects produced, clinically manifested by mental depression, vomiting, and urinary complications; the deviation of an enzyme by the sulfa drug in competition with *p*-amino-benzoic acid results in a hold-up of the building up process of the body of the pneumococci; as this enzyme is also essential in the metabolism of the build up of the human tissue it follows that an excess of sulfa drugs will upset this normal process by deviating too much of the enzyme. The constitutional upset is to be explained by this excessive enzyme deviation; carried to excess, this deviation could retard human tissue build up. In the case under review, it was argued that if an excessive dose was administered within a short time, infection could be overcome and yet the body tissue build up would not be upset too violently; the rapid excretability of the drug would also ensure this.

The treatment actually given was:—

Nursing in an open ward.

Glucose saline by drip method as described above for 72 hours.

Continuous oxygen for 48 hours.

Sedatives at night, and during day for first 72 hours, and thereafter at night only.

Diet of 1,800 calories daily for first 48 hours, chiefly milk and glucose saline.

Sulphapyridine—One gramme of daganan 4 hourly for 24 hours intravenously. One gramme by mouth 4 hourly for 24 hours starting 2 hours after the first daganan injection, thus ensuring a 2-hourly dose of one gramme for the first 24 hours.

Together with each oral dose of the drug, sodium bicarbonate grains 40 and sodium citrate grains 30 were also given. This was to prevent the urine from becoming unduly acid which might have caused crystallization of the drug in the urinary tract.

The first dose of sulphapyridine was given at 1130 hours on the first day and by 12 noon the next day the patient was much better. For the next 24 hours the intravenous medication was omitted and for the third 24 hours period 0.5 gramme of the drug was given 4 hourly. The total given was 6 grammes intravenously and 15 grammes by mouth. The patient made an uninterrupted recovery. Cyanosis was not noted, nor would it be expected with such a low hæmoglobin figure, and even if noticed it would not be a bar to continuing the drug.

The leucocyte counts during treatment were :—

Day of illness	Time	Total	GRANULOCYTES			Mono.	Lympho.
			Neutro.	Eosin.	Baso.		
2nd	1200	2,600	1,638 (63)	13 (0.5)	0	0	949 (36.5)
3rd	1000	2,450	1,446 (59)	24 (1.0)	0	0	980 (40.0)
4th	1000	2,600	1,534 (59)	26 (1.0)	0	0	1,040 (40.0)
5th	1100	2,650	1,538 (58)	26 (1.0)	0	26 (1.0)	1,060 (40.0)
8th	1200	3,000	1,950 (65)	15 (0.5)	0	30 (1.0)	1,005 (35.5)
15th	1000	6,500	4,420 (68)	65 (1.0)	0	65 (1.0)	1,950 (30.0)

The figures in brackets indicate percentage of the total count.

After this the anæmia was treated on appropriate lines which included a complete quinine-mepacrine-pamaquin course against malaria and one whole blood transfusion of 400 c.cm. On discharge from hospital 11 weeks later the blood showed hæmoglobin 15.5 grammes, red blood cells 5.28 million, and white cells 7,200; neutrophils—4,896 (68), eosinophils—144 (2), monocytes—72 (1), and lymphocytes—2,088 (29).

Followed up for seven months the patient's general condition has remained good. The hæmoglobin level was 14.8 grammes; leucocytes were 7,800 per c.mm. with normal distribution amongst the various types.

Commentary.—The risk of agranulocytosis has probably been exaggerated, an exaggeration caused by the seriousness of the complication; it probably did not exist in this case. The mode of administration did not give enough time for it to develop. Whether giving so large a dose was risky or not is debatable. Conclusions from, *in vitro*, experiments are often fallacious in this group of drugs and any enzyme deviation must have been too temporary to cause any lasting damage to the body. Judging by the follow-up, no harm was done; the results have amply justified the risks taken, if there really were any risks.

As a precautionary measure a large amount of sodium pentose nucleotide was kept handy. It might have been given concurrently with the sulphapyridine in anticipation of agranulo-

cytosis; but the fact that nothing untoward happened would appear to be a justification of the hypothesis on which the use of the large dose of the drug was based.

Summary

1. Treatment of a case of lobar pneumonia complicated by severe anæmia is described.
2. Some principles of sulfa drug therapy are discussed.
3. It is pointed out that a low granulocyte count need not necessarily be a deterrent to giving sulfa drugs.
4. Treatment of the anæmia does not form any part of this paper.
5. The case incidentally shows the tremendous reserve power of the human body.

It should be added that penicillin, if available, is preferable in such cases.

Thanks are due to Lieut.-Colonel Haridas, I.M.S., the Officer Commanding, for permission to report this case.

OCULAR MANIFESTATIONS OF AVITAMINOSIS IN ADULTS

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In the year 1943, 787 cases of avitaminosis with ocular symptoms were seen in the ophthalmic department of Indian Prisoners of War Hospital, Karanji, in Singapore, an analysis of findings in 500 of these cases forms the basis of observations made in this article. The first 100 cases have been taken from amongst those who reported for treatment in the months of January and February; the next 100 from amongst those who came in April and May; and the last 300 from amongst those who came after April. The reasons for this selection will be clear later.

It may be frankly admitted that neither the author nor any of his assistants had any previous experience in cases of avitaminosis. Moreover, being prisoners of war, and that too in the hands of the Japanese, they had neither

free access to any literature nor any reasonable facilities for diagnosis and treatment. The equipment in the hospital was meagre and mostly improvised, and the methods followed had to be rather primitive.

The ages of the cases seen varied between 21 and 58 years; but the great majority were between 30 and 40 years of age.

Most of the cases seen were suffering from deficiency of vitamin A and/or vitamin B. In the series under report, however, only one case of vitamin C deficiency was seen with massive subconjunctival hæmorrhage which was successfully treated with ascorbic acid. No further mention of this vitamin appears necessary in relation to the present series of cases.

Working system adopted

Due to want of previous experience and lack of adequate facilities as mentioned before, the cases admitted during the first two months could not be definitely labelled as due to specific vitamin deficiency, and they were treated mostly on the principle of trial and error. Symptoms and signs were, however, carefully noted, and the progress and response to treatment recorded. Articles available for administration in the treatment were fermented rice water, rice polishings, red palm oil, and a limited stock of marmite. Patients were advised to purchase eggs, peanuts and some fruits at their own cost but very few, if any, could afford them.

One hundred consecutive cases from amongst those admitted in January and February were analysed and the result of treatment by this trial and error method assessed. These results were :—

Limits of duration of treatment .. 2 to 17 weeks.
Number cured completely .. 78 Average period of treatment 6.3 weeks.

Number cured partially .. 10 Average period of treatment 5.1 weeks.

Number not improved at all .. 12

During these two months some ideas were gained about the combinations of signs and symptoms and it was presumed that these combinations may be ascribed, each to specific vitamin deficiency. The line of work was then modified with the intention of further amplifying and confirming these combinations, etc. Certain charitably disposed civilians or non-prisoners of war donated some money to purchase some supplementary articles of food, and by a stroke of good luck some condensed milk and red palm oil were made available for ophthalmic cases.

With the kind co-operation of Major Elahi Baksh, I.M.S., three diets were worked out from available materials, designed to provide vitamin A, vitamin B₁ and riboflavin respectively. These diet supplements were as follows :—

Diet supplements (I) Rich in vitamin A

Articles	Daily quantity	Vitamin A, I.U.	Vitamin B ₁ , I.U.	Riboflavin, mg.
Red palm oil ..	2 dr.	8,500
Fish in ration ..	2½ oz.	?	40	?
Bananas ..	Two (approximately 4 oz.).	700	24	0.20
TOTAL VITAMINS ..		9,200	64	0.20

It will be seen that vitamin B₁ and riboflavin in this supplement I are much below the level of daily minimal requirements for an adult, but vitamin A is abundant. In supplement II, vitamin B₁ is abundant but vitamin A and riboflavin are reduced to a low level or nil.

(II) Rich in vitamin B₁

Articles	Daily quantity	Vitamin A, I.U.	Vitamin B ₁ , I.U.	Riboflavin, mg.
Rice polishings ..	2 oz.	..	400	..
Fermented rice water.	1 lb.	..	?	..
Fish in ration ..	2½ oz.	..	40	..
Peanuts (raw) ..	4 oz.	..	400	1.02
TOTAL VITAMINS	840	1.02

There was some difficulty in attaining the desired level with regard to riboflavin; out of the articles available, none could afford the desired quantity of riboflavin without a corresponding increase in vitamin A and vitamin B₁. The following supplement was the best that could be prepared.

(III) Rich in riboflavin

Articles	Daily quantity	Vitamin A, I.U.	Vitamin B ₁ , I.U.	Riboflavin, mg.
Milk (condensed) 1/5 dil.	1 lb.	140	24	0.80
Fish in ration ..	2½ oz.	?	40	..
Kongkong (water-cress).	8 oz.	330	86	2.30
Bananas ..	Two (approximately 4 oz.).	700	24	0.20
TOTAL VITAMINS ..		1,170	174	3.30

Cases treated by these diet supplements showed improvement in a certain group of symptoms; some however showed a set-back, inasmuch as they started manifesting symptoms

and signs attributable to deficiency of the vitamin wherein the particular supplement on which they were put was poor. Thus, by rather rough and crude therapeutic experiments the groups of symptoms and signs were further amplified, modified and confirmed. The setbacks, however, made longer treatment necessary.

All cases admitted during April and May were treated by putting them on suitable supplement. One hundred consecutive cases out of these have been analysed and results assessed as under :—

Limits of duration of treatment ..	1 to 16 weeks.
Number completely cured ..	82
Number partially cured ..	8
Number not improved ..	10
	Average duration 5.1 weeks.
	Average duration 3.8 weeks.

It will be noticed that there is a slight improvement in the results as compared with those obtained in the first series of 100 cases, both as regards the percentages of cures and the duration of treatment.

Basic and accessory supplements

During treatment with the three diet supplements it was found, as mentioned before, that some cases developed complaints other than those which they had to start with. These were attributed to the deficiency of the vitamin which was deficient or absent in the particular supplement on which these patients were put. New symptoms developed, necessitated a change in treatment and this meant delay in discharging the patient. To obviate this, a basic diet was prepared, ensuring the administration of daily minimal requirements of all the three vitamins, irrespective of what particular deficiency the patient was suffering from; to this diet were added supplements in individual cases, so as to increase the quantity of the specific vitamin deficiency which was responsible for the individual patient's conditions. All patients admitted from May onwards were treated on these basic and accessory supplements.

Basic supplement

Articles	Daily quantity	Vita-min A, I.U.	Vita-min B ₁ , I.U.	Ribo-flavin, mg.
Red palm oil ..	1 dr.	4,250
Rice polishings ..	1 oz.	..	200	..
Peanuts ..	1 oz.	..	100	0.25
Kachang Hijau ..	1 oz.	..	300	1.48
Kongkong ..	6 oz.	250	65	1.73
TOTAL VITAMINS ..		4,500	465	3.46

Kachang Hijau is a Malay name for a green coloured cereal used as an article of food like 'dal'. Kongkong is a leafy vegetable which grows in abundance in marshy places and is very much like watercress.

Extra quantities of articles mentioned in the basic supplement and some additional articles were included in the accessory supplements for use in cases of deficiency of vitamin A, vitamin B₁ and riboflavin respectively. These accessory supplements are given below :—

(I) Accessory supplement for vitamin A deficiency

Articles	Daily quantity	Vita-min A, I.U.	Vita-min B ₁ , I.U.	Ribo-flavin, mg.
Red palm oil ..	2 oz.	8,500
Rice polishings ..	1 oz.	..	200	..
Peanuts ..	1 oz.	..	100	0.25
Kachang Hijau ..	1 oz.	..	300	1.48
Kongkong ..	6 oz.	250	65	1.73
Bananas ..	Four (approximately 8 oz.).	1,400	48	0.40
TOTAL VITAMINS ..		10,150	713	3.86

Accessory supplement for vitamin B₁ deficiency

Articles	Daily quantity	Vita-min A, I.U.	Vita-min B ₁ , I.U.	Ribo-flavin, mg.
Red palm oil ..	1 oz.	4,250
Rice polishings ..	2 oz.	..	400	..
Fermented rice water.	1 lb.	..	?	..
Peanuts (raw) ..	3 oz.	..	300	0.75
Kachang Hijau ..	1 oz.	250	3,000	1.48
Kongkong ..	6 oz.	250	65	1.73
Pine-apple ..	1½ lb.	?	135	..
TOTAL VITAMINS ..		4,500	1,200	3.96

(III) Accessory supplement for riboflavin deficiency

Articles	Daily quantity	Vita-min A, I.U.	Vita-min B ₁ , I.U.	Ribo-flavin, mg.
Red palm oil ..	1 dr.	4,250
Rice polishings ..	1 oz.	..	200	..
Peanuts (raw) ..	3 oz.	..	300	0.75
Kongkong ..	8 oz.	330	86	2.30
Kachang Hijau ..	2 oz.	..	600	2.96
Milk ..	8 oz.	70	12	0.40
Bananas ..	Six (approximately 12 oz.).	2,100	72	0.60
TOTAL VITAMINS ..		6,750	1,270	7.01

The quantities of vitamins in rations issued to the prisoners of war were negligible. The

articles mentioned in the foregoing supplements were supplied by private arrangement, and the cost was borne partly by the patients and partly out of the funds collected from charitably disposed persons.

Three hundred consecutive cases put on this line of treatment with basic and accessory supplements gave the following results :—

Limits of duration of treatment.	..	1 to 10 weeks.
Number completely cured.	255 (85%)	Average duration 3.9 weeks.
Number partially cured	24 (8%)	Average duration 3.6 weeks.
Number not improved	21 (7%)	

The results recorded above show an encouraging improvement over those in the first and second lots of cases both in the percentages of cure and in the duration of treatment.

From these therapeutic experiments it was deduced that vitamin A deficiency, vitamin B₁ deficiency, and riboflavin deficiency gave rise to three well-defined clinical pictures respectively. These pictures are detailed hereunder.

CLINICAL PICTURES

Vitamin A deficiency

Out of the 500 cases forming the basis of this article, 159 suffered from vitamin A deficiency. The chief complaints of these cases were night blindness—inability to see in the dark. Some of these cases complained of impaired vision during day as well, but difficulty in seeing in the night was stated to be definitely more troublesome.

A few cases (5 to 6 per cent) gave a history of some skin trouble—generally itching all over the body. Not a single case was, however, seen either with actual lesions or with history of any follicular lesions on the antero-lateral aspect of thighs, the posterior aspect of arms, shoulders, neck, back or face.

Itching of the eyes, and a feeling of dryness were frequently admitted. About 3 per cent cases had one or more meibomian cysts in the lids and varying degrees of blepharitis were present in 5 per cent cases.

The cornea was insensitive in 81 per cent of cases and keratinizing epithelial metaplasia was observed in some of them. A few cases of disciform keratitis (2 per cent) and few more with sclerosing keratitis (2 per cent) were seen. Only one case in the whole series had phlyctenular kerato-conjunctivitis. The resulting opacities in all these cases, as well as in those with corneal ulcers, became faint after the acute stage was over but did not disappear completely.

About 2 per cent cases developed corneal ulcers. These responded well to local application of red palm oil. They manifested marked lacrymation and photophobia, but pain was remarkably absent altogether or was very slight indeed.

Not a single case showed xerosis or keratomalacia.

The pupils tended to be dilated in all these cases, but the reaction to light was brisk. Ocular tension was practically normal in all cases.

The fields of vision (tested by hand movements) showed marked concentric contraction, with what amounted to 'tubular' vision in advanced cases. One assumed that dilatation of pupils may be an effort on the part of nature to overcome to some extent the effect of the contraction of field of vision.

Visual acuity for distance was found reduced in all cases. In early cases the reduction in the central visual acuity was only slight compared with the reduction in the fields of vision; in more advanced cases, however, the reduction in central visual acuity became marked, but still it was less than the reduction in the field of vision. These patients in the advanced stages complained that lately their sight in the day also had started failing in addition to night blindness.

Impairment of vision in the night presented certain interesting features which helped in distinguishing it from nyctalopia due to other causes. Night blindness in these cases preceded the failing of vision in day as mentioned above. In dark nights the patient had great difficulty in moving about, as he could not see the ground in front of him clearly, and could not distinguish elevations and depressions; looking at the sky, however, he could see the stars more or less clearly; moonlight afforded him some relief in moving about; bright electric light gave him the best vision, but the adaptation to darkness was greatly delayed.

Reading and near vision in early stages was apparently unaffected; in later stages, however, the patients had some difficulty in reading, particularly in dim light.

Ophthalmic examination revealed that the media were quite clear and the fundi appeared normal.

Thiamin (vitamin B₁) deficiency

Two hundred and twenty out of the 500 cases under report were thiamin deficiency cases. Their chief ocular complaint was dimness of vision—inability to recognize faces from a distance of 20 or 30 yards. Literate patients complained of difficulty in reading.

There was no history of any skin lesions. Most of the patients complained of a burning sensation in the feet and hands. Only a few were cases of advanced dry beri-beri.

A burning sensation in the eyes, a dull pain in the back of the eyeball, discomfort on exposure to sunlight, lacrymation, mild photophobia with some degree of blepharospasm were present in almost all the cases.

The conjunctiva and cornea were practically normal in appearance; the pupils were normal in size or slightly contracted, briskly reacting

to light but sluggish or inactive to accommodation, the reverse of the Argyll Robertson pupil. Intra-ocular tension tended to be increased.

Visual fields showed mild peripheral contraction; central visual acuity was reduced—the reduction was more marked than the contraction of the field of vision; accommodation power was weak, and near vision was consequently tiring, simulating premature and rapidly progressing presbyopia. Some patients were actually using rather indiscreetly prescribed convex glasses for reading and close work.

Ophthalmoscopic examination revealed clear media and normal fundi except in 2 per cent of cases manifesting signs of optic nerve atrophy. These latter were incidentally well-advanced cases of dry beri-beri, with muscular atrophy well set in; intra-ocular tension in these was definitely raised; they did not improve with treatment and the damage done was permanent.

Visual disturbance in all cases, both for distant and for near work, was equally marked during day and night.

Riboflavin deficiency

Cases of riboflavin deficiency—121 in the 500 under report—complained chiefly of hazy vision in the sun. They said they saw as if there was a screen of smoke. In cloudy weather or at dusk and dawn, they could see more clearly and felt easier.

Nearly 78 per cent of these cases gave a history of exfoliative or seborrhœic dermatitis in groins, scrotum, and medial sides of the thighs, about 4 to 8 months prior to the onset of visual symptoms. Only a few showed erythematous base or greasy desquamation in the naso-labial fold or on the *alæ nasi*, but the rest of the face and posterior aspects of the ears were free in all cases.

Practically all the cases had well-developed patches of cheilosis-discoloration of the mucous membrane at the angles of the mouth, with maceration and superficial cracks extending to the adjoining cutaneous aspect 'angular stomatitis.' Patients took no notice of these patches, as they caused no discomfort except the disfiguration. As the æsthetic sense had been completely dulled in the prisoners of war, the disfiguration was ignored.

All the cases denied having any pain or itching in the eyes, but some admitted having a burning sensation. In practically all cases, the conjunctiva showed a streak of vascular injection in the interpalpebral region, extending from the limbus laterally to the outer canthus. At the outer canthus were also seen superficial cracks extending to the cutaneous surface. These gave an appearance of angular conjunctivitis.

The cornea was found clear in all cases except one, which showed sclerosing keratitis with circumcorneal injection. This injection

and the corneal vascularization cleared under treatment, but localized 'haze' in the deep layers of cornea persisted.

The pupils were moderately dilated and sluggish in reaction to light unlike the pupils in vitamin A deficiency when they were dilated but reacted normally to light. The visual discomfort in the sun and bright light may be attributed to dilated sluggishly reacting pupils.

The central visual acuity for distance was reduced, but the accommodation power was practically normal, and reading and close work could be attended to without much difficulty. In this respect the cases superficially simulated myopia—'pseudomyopia' was the name given to this condition. Some of them were actually using indiscreetly prescribed concave glasses. These glasses helped to sharpen the outline of objects but did not actually increase the visual acuity.

Ophthalmoscopy revealed no abnormality either in the media or in the fundi.

The fields of vision showed contraction in the upper and temporal regions but were normal in the nasal and lower regions in the early stages; in advanced cases the contraction of the fields of vision involved the lower and nasal regions as well, and ultimately the contraction was marked in all regions so that it resembled the contraction in vitamin A deficiency cases. At this stage the patients complained of impairment of vision in night as well: the visual acuity for distance was also proportionately reduced. Nyctalopia having been added to the symptoms at this advanced stage, the patients felt better in daylight than in the night.

In these cases with nyctalopia added, there was some difficulty in distinguishing them from vitamin A deficiency cases in earlier months of the experiments: later, however, when the differentiating features had been fully worked out, there was no difficulty.

The nyctalopia of riboflavin deficiency was a later symptom, preceded in the early stages by hemeralopia; the pupils in these cases were dilated as in vitamin A deficiency cases, but unlike the latter, they reacted briskly to light. On dark nights patients found it difficult to move about and find their way, like vitamin A deficiency cases, but unlike the latter, they could not see the stars in the sky; they felt most comfortable in moonlight but, unlike the vitamin A deficiency cases, they felt very uncomfortable in bright electric light and tried to avoid looking directly at a flame or source of light. The reduction in the visual acuity in these cases was proportionate to the reduction in the fields of vision.

These cases showed no improvement on red palm oil and vitamin A rich supplement.

Associated conditions

Fifty-one per cent cases in the series under report were in the habit of smoking cigarettes; 1 per cent chewed tobacco and 1 per cent

smoked 'huqqa.' It was suspected that tobacco amblyopia may be an aggravating factor in the visual symptoms. About 8 per cent cases were purely cases of tobacco amblyopia. Most of the smokers had dirty conjunctiva; the pupils were normal in size and reactions; the peripheral fields of vision were practically normal and the optic disc in some cases showed temporal pallor. In testing the visual acuity of these cases an interesting feature was observed, i.e. they invariably confused letters in several successive lines of the chart before reaching the line they could not read; thus they are superficially simulated cases of astigmatism; some of them were using astigmatic corrections with equally indiscreetly prescribed concave glasses.

All the smokers were advised not to smoke. The great majority agreed to submit to the regime but a few insisted on continuing the

habit. Such cases of genuine tobacco amblyopia did not give up smoking, showed no improvement in spite of their being put on vitamin B₁ rich or on any other supplement. This result does not coincide with the opinion of Yudkin and Carrol who claim to have treated cases of toxic amblyopia (tobacco and alcohol amblyopia) with vitamin B₁, allowing the patients to continue smoking and drinking moderately, and got excellent results.

In the preparation of this article, very little literature could be consulted as none was freely accessible in the prisoners of war camps. By the co-operation of certain friends in the vicinity and the prisoners who used to go out of the camps for fatigues, the following were smuggled in and were of great help.

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A Mirror of Hospital Practice

PENETRATING INJURY IN A PREGNANT WOMAN

By P. R. SURI, M.B., B.S.
District Hospital, Moradabad

A MULTIPARA, 30 years, 8 months pregnant, sustained injury due to a fall from a staircase from a height of 25 feet, and was reported to have bled profusely per vagina. No further details of the fall were available. The patient was in a state of severe shock and almost pulseless, looking blanched and exsanguinated.

Vaginal examination showed intense bruising, tenderness, and swelling of the labia and the inner side of the left thigh. Morphia was given to combat shock, and to check bleeding, hæmostatics were given and the vagina was packed. Two pints of serum were given by transfusion.

The patient's general condition improved. A second vaginal examination, under anaesthesia, revealed a big lacerated tear in the right wall of the vagina going deep through the right fornix. Efforts to clamp and ligature the bleeding points failed as some big venous sinuses appeared to have been torn. Deep stitches were therefore inserted on both sides, the wound was packed and a tight binder given. The patient's general condition again became very low. Two pints of whole blood were given by transfusion, the first pint at a continuous rate and the second at 80 drops per minute. The pulse and colour returned gradually.

Next morning labour pains started; these were temporarily controlled by sedatives. Repeated examinations failed to show any audible heart sounds, and the patient herself complained of cessation of all foetal movements. Labour again set in within the next 12 hours, but fortunately the bleeding was not severe and a dead female child was born.

The patient's general condition again became low. Transfusion of one pint of serum and 1½ pints of blood was given at a slow rate of 40-20 drops per minute. The temperature rose up to 102°F. indicating sepsis of wound; this was treated by sulphanilamide, soluseptaine injections and vaginal douches, and painting with mercurochrome. The patient has since completely

recovered, except for a prolonged convalescence on account of severe anæmia.

My thanks are due to the Lieut.-Colonel G. D. Malhoutra, I.M.S., Civil Surgeon, Moradabad, for guidance in treatment and for permission to publish this report.

PURPURA CAUSED BY VITAMIN K DEFICIENCY

By P. N. LAHA

and

B. P. KACKER

(From the Department of Diseases of Children, Medical College, Agra)

PURPURA is a condition whose chief feature is a tendency to bleeding into the skin and from the mucous membranes. It can occur in diverse diseases. Broadly speaking, it can be classified as secondary or symptomatic purpura on the one hand, and primary thrombocytopenic purpura on the other. Deficiency of vitamin K as a cause for this condition is rare, and the following case will therefore be of interest.

A Muslim male child, aged 7 years, was admitted into the children's ward with complaints of bloody stools for four days and epistaxis for one day. The onset was sudden and febrile. There was a history of a similar attack a year ago.

On examination, the patient was markedly pale; temperature 100°F.; pulse 110 and respiration 20 per minute. There were epistaxis, bloody stools, purpuric patches on the body and right-sided subconjunctival hæmorrhage; spleen not palpable, liver not enlarged. Clinical examination revealed no abnormality in any system.

Blood examination.—Rh negative; culture sterile, tourniquet test negative; results of blood count, etc., before, during and after treatment are given in the table appended.

Stool and urine showed no abnormality.

Progress and treatment.—Injections of hæmostatic serum 5 c.cm. intramuscularly, vitamin C 400 mg., and 5 c.cm. of 10 per cent calcium gluconate intravenously were given for four days with no appreciable improvement. Blood transfusions were then started, 20 c.cm. on alternate days, the donors being the parents, the mother being Rh negative. The hæmorrhage stopped after the second transfusion. The results of blood examination after five transfusions (total quantity 160 c.cm.) are shown in the table. Two days later, severe epistaxis occurred in the night. Blood was again examined (*see table*).

Results of blood examination before, during and after treatment

	Total r.b.c.	Total w.b.c.	Hæmo- globin, g.	Poly- morphs	Lympho- cytes	Large mono- cytes	Eosino- phils	Coagula- tion time, min.	Bleeding time	Platelet count
Before treatment ..	3.1	13,800	6.0	89.0	9.0	1.0	1.0	9.0	min. 2 sec. 3	175,500
After 5 transfusions ..	2.99	5,000	6.5	67.0	31.0	2.0	..	3.20	2 5	195,000
Two days after above examination.	2.28	3,500	5.0	49.0	50.0	1.0	..	3.10	2 5	180,900
After vitamin K treat- ment.	3.1	5,010	9.0	39.0	52.0	9.0	..	3.20	2 30	201,500

In spite of the treatments, the patient was having occasional attacks of slight epistaxis, purpuric patches on the body and bleeding per anum. At this stage the prothrombin time of blood was found to be 56 seconds and the Takata-Ara test was positive (in 1/8, 1/16, 1/32, 1/64 dilutions after 24 hours). Purpura was ascribed to vitamin K deficiency. The patient was given kapilin 10 mg. tablets, one thrice daily, and ferrostol one tablet three times a day. After 10 days of this treatment, the prothrombin time was 32 seconds. The results of blood examination done after another 18 days are shown in the table. There was no further recurrence of bleeding from any source. The Takata-Ara test was negative and prothrombin time 36 seconds.

The vitamin K deficiency in this case was probably due to hepatic dysfunction as evidenced by the positive Takata-Ara test which became negative afterwards.

Our thanks are due to Major-General H. C. Buckley, I.M.S., Principal, Medical College, Agra, for permission to report the case and to our colleagues in the department of pathology for their help in the investigation.

A CASE OF BRUCELLOSIS (ABORTUS FEVER)

By M. S. H. MODY, M.B., B.S., M.R.C.S., L.R.C.P.,
D.T.M. & H.

STRAY cases of brucellosis are met with, and one generally remembers to exclude undulant fever as a probable condition in those cases of long-continued pyrexia, where the common or garden causes of it are excluded; yet, I believe, abortus fever in man, caused by *Brucella abortus*, is not kept in mind when investigating a case of P. U. O., hence the following description of a case of abortus fever, I hope, will not be out of place.

P. A. M., Hindu, aged 43 years, was sent to me by his doctor from his village of Malshiras in Sholapur district for fever which he had been running for exactly fifty days and which had been considered clinically

enteric and treated as such. He was admitted under my charge, in the Sassoon Hospitals, on 5th January, 1946. On admission his temperature was 102, pulse 112, and respirations 24, and despite his long-continued pyrexia of nearly two months his physical condition struck me to be remarkably good, and his mental condition very alert.

Physical examination revealed fairly good colour and nourishment, a clean and moist tongue very unlike the typhoid tongue, good appetite, and excellent memory as judged by the way he gave the history of his illness. Nothing pathological in the respiratory

and cardiovascular systems. Blood pressure 120/70. Teeth rather dirty and a normal throat, tonsils had been removed by operation. Abdomen soft and not distended, with no enlargement of the spleen but the hepatic border palpable with one finger enlargement of the liver. No abdominal tenderness elicited.

There was complete absence of enlargement of the glands anywhere, nor were any joints painful or swollen. Central nervous system was normal. Careful search failed to find any skin rash.

Screening confirmed normal and healthy lungs, pleura, mediastine, heart and aorta. There was no upward enlargement of the liver and movements of the diaphragm on both sides were equal and good.

Blood examination.—Wassermann reaction negative, malaria parasite absent, white cells 12,500 per c.mm., polymorphonuclears 63 per cent, lymphocytes 34 per cent, large mononuclears 3 per cent, eosinophils 0 per cent. Widal negative for TAB.

Urine showed nothing abnormal chemically or microscopically.

A radiogram of the chest was taken two days later, and it was quite normal.

As he was running a temperature with the hepatic enlargement as the only finding, he was put on $\frac{1}{2}$ gr. emetine injections, and glucose with 500 mg. of vitamin C was given intravenously. As three grains of emetine did not produce any effect on the temperature it was discontinued.

Up against a blank wall for diagnosis and taking into consideration his profession of a veterinary surgeon Dr. Munshi, the pathologist to the hospital at my request carried out blood agglutination tests for undulant and abortus fever, as well as blood culture. The cultures were reported sterile, agglutination tests for 'T. O.', 'T. H.', para A. O., and para B. O., were once again negative, but agglutination against *Brucella abortus* was found to be positive in 1 in 200, on the 24th January, 1946, which was repeated on the 9th February, and found positive in a higher dilution of 1 in 500. This proved the case to be one of abortus fever.

There being no specific treatment for it, and the organism being non-sensitive to penicillin, sulphapyridine was tried, but as the patient showed signs of severe intolerance, to both oral and parenteral administration, it was stopped. Intravenous injection of TAB vaccine was refused by the patient, and hence it was not tried in this case.

He continued to have irregular bouts of fever with short periods of remissions until his discharge from hospital on the 19th March, 1946, the total duration of fever till then being nearly 120 days, *viz.* 17 weeks.

Abortus fever is a fever known to be usually of long duration and undulant in character, ranging in its duration from 3 to 40 weeks, with an average of 12 to 13 weeks. It is caused by infection with *Brucella abortus*, the organism which is responsible for contagious abortion in cattle. Human infection is due to contact with infected cattle or consumption of infected milk.

E. Creed in the *British Encyclopædia of Medical Practice*, Vol. I, writes that Wilson found that 20 per cent of the practising veterinarians in England had agglutinins for *Brucella abortus*, and were therefore probably cases of latent infections. He goes further and says that the incidence of undulant fever in England and Wales, as judged from a study of the presence of abortus agglutinins in Widal sera, is estimated to 500 cases a year.

My thanks are due to Major H. Smithwick, I.M.S., Superintendent, Sassoon Hospitals, Poona, for publication of this case.

MISTAKEN DIAGNOSES

By T. D. RAJOO

CASE REPORTS

(1) *Chocolate cysts of the ovary*

Mrs. M., aged 20 years, married six months ago, was admitted for severe pain in the lower abdomen followed by red discharge per vagina since the previous night. The last period was 25 days ago. General condition good. Pulse 90 per minute. Heart and lungs nothing abnormal detected. P.V.—Os closed. Uterus pushed to the right by a slightly movable tender swelling in the left and posterior fornix. No pulsation felt. No discharge on examining fingers. On questioning, the patient said she always suffered from dysmenorrhœa. Blood pressure 100/70. White cells 12,000 per c.mm. Red blood corpuscles 4,250,000 per c.mm. Hæmoglobin value 75 per cent. Colour index 0.8.

As the provisional diagnosis of ectopic gestation was in doubt, a needle was put in the pouch of Douglas and dark-brown blood was drawn into the syringe. Diagnosis of ectopic gestation was confirmed and the patient readily consented for operation.

No free blood was found on opening the abdomen in the peritoneal cavity. The left ovary was fixed to the back of the uterus and sigmoid colon and was of the size of a tennis ball. The right ovary was also cystic and of the size of a lemon and not adherent to the surrounding tissues. While separating the left ovary from its attachments, the cyst ruptured discharging dark-brown blood. A thick needle was put in the right cystic ovary and it also contained dark-brown blood. Even here it was found difficult to resect the cyst and therefore the right ovary was also removed. Patient was discharged cured.

Wilfred Shaw says chocolate cysts of the ovaries are bilateral in about a third of all cases. If both ovaries are affected by 'chocolate cysts', the two ovaries must be removed, and if there is pelvic endometriosis or adenomyosis of the uterus, a hysterectomy has to be performed.

(2) *Dermoid cyst of the lung*

A male, aged 18 years, was admitted for fever and cough for four days (?) and pain on the right side of chest for about a year. At the time of admission temperature was 101°F. Pulse 120 per minute. Physique poor. Apex beat of the heart slightly pushed to the left. Bulging of the right chest. Breath sounds could not be heard on the right side. No cyanosis, no clubbing of the fingers. No vomiting.

White cells 15,000 per c.mm. Polymorphonuclears 70 per cent. Lymphocytes 26 per cent. Mononuclear 2 per cent. Eosinophils 2 per cent. X-ray showed complete opacity on the right side of chest. Wassermann reaction negative.

Patient was taken to the theatre and a jelly-like substance was aspirated from the right side of chest. Diagnosis: 'Hydatid cyst'. The substance was sent to the laboratory for report. No scolices or hooklets to be seen. Casino's test was not done for want of antigen. Two days later patient developed rash on the right side of chest. After a few days resection of the ribs was done and when the pleura was opened there was hæmorrhage and the lung was found hard with small pieces of bone. Patient's condition became bad and after packing with gauze the wound was closed. Patient died the next day. On post mortem the pleura was very thick and the whole lung was found hard containing hair and bones.

William Boyd says that mediastinal dermoids are rare tumours found in the mediastinum or within the lung. These growths are probably derived from third branchial cleft. These tumours are usually cystic and the cysts are lined by all the elements of the skin, epidermis, dermis and dermal glands. Additional structures such as bone cartilage, lymphoid tissue and fat may be present. The cysts may be filled with sebaceous material produced by the glands in the wall.

Clinical diagnosis was effusion; after aspiration hydatid cyst, and after resection dermoid cyst of the lung.

I am grateful to Colonel M. R. Atkinson, I.M.S., for allowing me to report these cases.

A CASE OF 'SCINTILLATIO ALBESCENS' (HYVERNAT-BENSON'S DISEASE)

By MARIO STEFANINI, M.D. (Rome)

'SCINTILLATIO ALBESCENS' was first described by Hyvernât in 1880. Benson (1894) distinguished the condition from 'synchysis scintillans' by the absence of fluidification of the vitreous and the consequent absolute or relative fixity of the bodies. Various authors have since described several cases (56 in the review of Rutherford, 1933), and the disease appears to be more common than is usually believed as its recognition, owing to the absence of subjective symptoms, is usually accidental in the course of routine examination.

Benson who gave a classical description ('small, smooth, fixed spheres of a light cream colour.....hundreds everywhere in the vitreous body, ranging in size as much as the stars in a frosty night') designated the condition as 'asteroid hyalitis.' However, no inflammatory changes have ever been described in

the vitreous body and the 'asteroid bodies' appear to be more a degenerative rather than an inflammatory product. Wiegmann called the condition 'scintillatio albescent', and morphologically divided it into two varieties: a type in which the asteroid bodies look like shining yellowish spots (a very rare condition) and a type in which the opacities appear as snow-ball white opacities, of spherical or irregular outline.

The condition does not cause any subjective symptoms, and it is usually discovered on ophthalmoscopic examination, when the asteroid bodies appear as 'white and shiny bodies as stars in a night sky' by reflected light and dark by transmitted light. In the beam of a slit lamp they look like dead white, round and brilliantly gleaming spheres. They have no orderly arrangement nor fixed place as they may be found scattered everywhere throughout the vitreous, anteriorly or posteriorly to the equator. They are fixed or moving with a wave-like, well-restrained excursion, and never fall to the bottom. More common in males than in females (3 out of 4 cases) and in very old people, the condition is usually unilateral (in 75 per cent of the cases).

The following case seems to be worth reporting for its medical peculiarities.

A male patient, aged 52 years.

Family history.—The father of the patient died when 64 years old from cerebral hæmorrhage.

Past history.—He had an attack of benign tertian malaria in 1924 without relapses. No history of syphilis.

Present history.—For the last four years the patient has been complaining of breathlessness after slight exertion, palpitation, precordial pain diffused to the inner side of the left arm, numbness of the left hand, nocturnal paroxysmal dyspnoea, polyuria and micturia, swelling of the ankles at night. During the last four months his symptoms have grown worse, and there has been a marked loss of weight during the last six months. The patient has been using spectacles for slight hypermetropia for 8 years; no other ocular symptoms.

Examination.—Poor general condition. Presence of long light-coloured scars over the buttocks and abdomen from loss of fat. Lymph nodes slightly enlarged, hard, but not tender. Temporal arteries serpiginous and hard. Pitting of the ankles. The apex of the heart is palpable in the sixth intercostal space along the mammary line. Pulsation of the aorta palpable in the jugular notch. First aortic sound covered by a slight murmur, especially evident after exertion; second aortic sound forcible and reduplicated. Blood pressure 165/102, pulse frequent, regular, equal and hard. Exertion causes a feeling of discomfort in the precordial area accompanied by numbness along the inner side of the left arm. Liver and spleen in normal limits.

Arcus senilis in both eyes. Vision 8/10, with +2.50 for the right and +3.25 for the left eye. Media clear in both eyes. The ophthalmoscopic examination shows silver wire arteries, elongated, compressing the veins at their crossings, of normal calibre. In the upper nasal quadrant of the right eye, presence of small, spherical, yellowish bodies, slightly moving and coming back easily to their original position, posterior to the equator.

Laboratory examination.—(1) Wassermann reaction—negative. (2) Renal function: no abnormalities in the urine; good dilution but deficient concentration by

Volhard-Rosenberg test. Blood urea: 52 mg. per cent plasma: Ambard's $K = 0.15$ and urea clearance (McIntosh-van Slyke) = 55 per cent of average normal. (3) Total blood cholesterol: 285 mg. per cent. (4) Blood count: red cell corpuscles 4,600,000; white cells 6,600; colour index 0.98; hæmoglobin (Sahli) 90 per cent. Differential count—neutrophils 65 per cent, eosinophils 2 per cent, monocytes 10 per cent, and lymphocytes 24 per cent.

Screening the chest.—Confirms the presence of an enlargement of the first part of the aortic arch.

Discussion

The ætiology and pathogenesis of this condition have been much discussed. Histopathological examinations are still very few and usually negative. Microscopical examinations of the asteroid bodies show that they are usually composed of masses of macrophages containing lipoids, or of giant cells including a central drop of fatty substance, or of gliomatous elements derived from the retinal epithelium. They are usually composed of calcium soaps. The tests for cholesterol, albumin and tyrosin are negative and those for sodium chlorides, and fatty substances are positive.

The cause of these deposits, either of local or of blood-borne substances, remains unknown. 'Scintillatio albescent' has been found associated with local (choroiditis, retinal hæmorrhages, thrombosis of the retinal vessels, cyclitis, traumata) and general conditions (arteriosclerosis, nephrosclerosis, diabetes, syphilis, tuberculosis, etc.). They all appear to be purely coincidental. As asteroid bodies are so frequently unilateral, local conditions probably play a great part in their pathogenesis, as shown by experiments on rabbits. Deposits of calcium oxalate in the vitreous occur in rabbits poisoned with naphthalene more easily if the vitreous has been rendered alkaline, and marked variations of the pH of the vitreous also appear to be responsible for precipitation of vitreous gels. In both cases precipitation of the proteins could occur if they reach their isoelectric point.

Both vascular lesions of the eye and (Wiegmann) excess of blood cholesterol may cause vascular troubles of the ciliary body and so determine, through defects of nutrition of the vitreous, precipitation of proteins. Most certainly the occurrence of the condition in healthy but aged eyes, while it does not support the idea of Benson of a congenital disease, seems to support the theory of vascular lesions due to age in constitutionally predisposed subjects.

These considerations would lead us too far. It will be enough to point out that the present case in a man, looking much older than his age, with widespread arteriosclerosis, is an example of a non-specific degenerative change.

I wish to thank Dr. Falcone Giuseppe, M.D., eye specialist, for his careful examination of the case.

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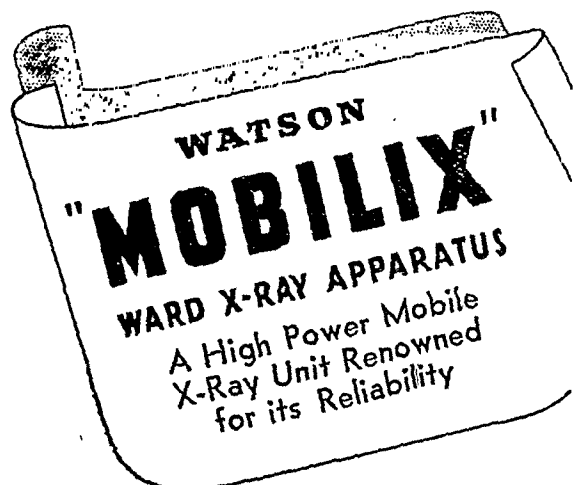
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Indian Medical Gazette

APRIL-MAY

THREE STATEMENTS ON THE HEALTH OF INDIA AND ASSOCIATED OBSERVATIONS

1. SIR JOHN MEGAW'S LECTURE.—

This observer in Sir George Birdwood Memorial Lecture (1946) states that he has studied the health situation in India with ever-increasing anxiety for 25 years. The country is heading for a calamity. Basic laws of health are being ignored. While full attention is being paid to prevention of infectious diseases the standard of living is allowed to remain low. As a result the population is increasing, the food supply is decreasing and the standard of living is going down further. Malnutrition is becoming chronic, working capacity is decreasing, food production is diminishing and distress is increasing.

Since the first census in 1872 the population has increased. For the first 50 years it increased at the rate of 4 per cent every 10 years. Since 1921 there has been a remarkable rise. In the 10-year period 1931 to 1941 the increase for the whole of India was 15 per cent and for some areas 19 per cent to over 22 per cent. In these latter areas, but for the limited food supply and ravages of infectious diseases, the population would have easily doubled itself in 30 years.

An optimistic view held by some was that public health efficiency would improve the standard of fitness and living and decrease the birth rate. A complacent view of the situation was taken up to quite recent times until the Bengal famine of 1943-44 caused a gasp of astonishment. A remarkable feature of the famine was that the actual shortage of food in 1943 was estimated as being only about 6 per cent. A curious sidelight on the situation is thrown by the Bengal Public Health Report for 1941 (issued in 1946). The death rate in that year was higher and birth rate lower than in 1940. This simultaneous deterioration in the death and birth rates was unusual. It had occurred before in 1938 and 1918. Explaining the 1918 deterioration by the pandemic of influenza the other two occurrences in rapid succession are suggestive of the approach of a critical level in the nutrition of the people.

Travancore is another part of India suffering from distress. The increase in its population during the 20 years, 1921 to 1941, was about 50 per cent. Here, even a high standard of literacy and philanthropy has not averted the inevitable consequences of ignoring the basic laws of health.

The root cause of the trouble is the outlook of the people. Attempts have been made in the past to set up an organization of non-technical experts familiar with the lives of the villagers to enquire into the social and psychological aspects of the question. These attempts have not succeeded. It is the social and other customs which play so important a part in the ill health and economic depression of the country. A new outlook on life must be created. This is, concludes Sir John, not a plan but a plan to prepare a plan which can be prepared only by educated Indians themselves.

2. REPORT OF THE HEALTH SURVEY AND DEVELOPMENT COMMITTEE UNDER SIR JOSEPH BHOORE.—The main principles underlying the committee's proposals for the future health development in the country, given in a 'nutshell' in the foreword to the volume IV which is a summary, are:—

1. No individual should fail to secure adequate medical care because of inability to pay for it.

2. In view of the complexity of modern medical practice, the health services should provide, when fully developed, all the consultant, laboratory and institutional facilities necessary for proper diagnosis and treatment.

3. The health programme must, from the beginning, lay special emphasis on preventive work. The creation and maintenance of as healthy an environment as possible in the homes of the people as well as in all places where they congregate for work, amusement or recreation, are essential. So long as environmental hygiene is neglected, so long as the faulty modes of life of the individual and of the community remain uncorrected, so long as these and other factors weakening man's power of resistance and increasing his susceptibility to disease are allowed to operate unchecked, so long will our towns and villages continue to the factories for the supply of cases to our hospitals and dispensaries.

4. The need is urgent for providing as much medical relief and preventive health care as possible to the vast rural population of the country. The debt which India owes to the tiller of the soil is immense and, although he pays the heaviest toll when famine and pestilence sweep through the land, the medical attention he receives is of the most meagre description. The time has therefore come to redress the neglect which has hitherto been the lot of the rural areas.

5. The health services should be placed as close to the people as possible in order to ensure the maximum benefit to the communities to be served. The unit of health administration should therefore be made as small as is compatible with practical considerations.

6. It is essential to secure the active co-operation of the people in the development of the health programme. The idea must be inculcated that, ultimately, the health of the individual is his own responsibility and, in attempting to do so, the most effective means would seem to be to stimulate his health consciousness by providing health education on the widest possible basis as well as opportunities for his active participation in the local health programme.

7. We consider it essential for the success of the scheme that its development should be entrusted to Ministers of Health who enjoy the confidence of the people and are able to secure their co-operation. Both in respect of legislation and of administration it is likely that some of the measures to be undertaken may offend existing social and religious practices, while others may involve control over the day-to-day life of the citizen. We therefore feel that it is only a Minister enjoying the confidence of the people who can carry such enactments through the legislature and ensure their practical application in the country.

The term health is made to imply 'more than an absence of sickness in the individual and indicates a state of harmonious functioning of the body and mind in relation to his physical and social environment, so as to enable him to enjoy life to the fullest possible extent and to reach his maximum level of productive capacity'.

The report consisting of survey, recommendations, appendices and summary is a masterpiece of exposition, proposition and details. It recognizes the faulty customs, habits and outlook of the masses, and suggests remedies. A plan desired by Sir John has been prepared by educated Indians.

On the population problem the report gives a warning but is neither pessimistic nor unhumanitarian. It does not suggest that the control of the infectious diseases should be relaxed to wipe out the excess of population. The percentage of increase is large but not larger than that of the United Kingdom for the same period (1872 to 1941, India 54 per cent and United Kingdom 56 per cent) and nowhere near that of Japan (same period, 136 per cent). The fact that the increase is a large addition to an already *vast population used to a low standard of living* is recognized: Hence the warning.

The possibilities of getting more food from the land and sea are considered likely. The control of disease, malnutrition and under-nourishment will raise the standard of fitness, the working capacity and the standard of living. The raised standard of living will lower the birth rate when the people realize that the attainment of the standard should come before the building of the family. Instructions in birth control will also be given.

'The doctor of the future should be "a social physician protecting the people and guiding them to a healthier and happier life."'

3. A SAMPLE SURVEY OF AFTER EFFECTS OF THE BENGAL FAMINE OF 1943 BY MAHALANOBIS AND OTHERS.—This document (Mahalanobis, Mukherjea and Ghosh, 1946) gives important local data, information which supports Sir John and raises new questions in the reader's mind.

The data are: (i) the average yield of rice in Bengal is about 10 maunds (820 lb.) per acre, (ii) the average size of the rural family is about 5.4, (iii) the average consumption of rice is about 4 maunds per head per year, and (iv) the subsistence level is 2 acres of paddy land per family.

The actual position in Bengal before the famine was one of distress. The overall average for the province as a whole was about 1.8 acre of paddy land per rural family which is below the subsistence level. The cattle position was not satisfactory. The total number of plough cattle in 1943 was 79 lakhs giving a share of $4\frac{1}{2}$ acres of paddy land per pair of

bullocks which is just adequate or falls slightly short of the requirement.

During the famine about one-fourth of the rural families which owned paddy land before the famine sold or mortgaged their land. The plough cattle decreased by about 13 per cent, mostly by sale again, possibly to the contractors for the supply of meat for army consumption.

Destitution in 1931 was 1.07 per cent. The figure ought to have given a population of 5.9 lakhs of destitutes in January 1943. The sample estimate was 7.5 lakhs. Thus, at the beginning of 1943, there had already been an increase of 1.6 lakhs of destitutes. Economic deterioration had set in definitely in the pre-famine period. The famine itself was the culmination of the deterioration.

The reader reflects.

Sir John sees the deterioration in the nutrition of the people of Bengal in 1941. The rest follows as predicted. How does Sir Joseph propose to get more food out of the land which definitely is below the subsistence level? Small holdings do not admit of intensive agriculture. Measures for reallocation of land are called for. Those who are dispossessed must be given other professions. If persuasion succeeds compulsion is not necessary.

Could the poorer agricultural classes have averted the famine if the families had not parted with their last few maunds of paddy for prices which appeared to them unprecedented at that time but which later could not buy enough until the next crop was brought in? The answer is, yes: the actual shortage of food was only 6 per cent. In their greed they sold all which was cornered and/or diverted. The cornering which was more disastrous of the two in its effects, because of the black market and uneven distribution of food, was made possible by the population pressure. With less population, and consequently abundant food, it would not have been worth the profiteers' while and would not, at any rate, have been so deadly. The famine was man-made and made by the rural families themselves in the first instance.

ASSOCIATED OBSERVATIONS.—The greed of the lower orders of the population in Asia, generally, and India, particularly, is tragic. The cash obtained by the sale of any commodity which is saleable is first hoarded and then wasted on (i) births, (ii) marriages and (iii) deaths. It does not raise the standard of living. So much zeal and energy are concentrated at these three short nodes in the life of a man and possibly a festival or two a year that no enthusiasm is available for the long internodes which are utterly neglected. Leisure and joy of living in these intervals are neither possible nor desired. In fact a life including leisure and joy throughout is regarded as a life of sin.

Of wealth the lower orders receive enough but it does not stay with them because of their

fitfully wasteful ways. *Lakshmi* does not stay in a house where she is not honoured (every day). The poverty of the masses in the East is not due to a lack of wealth but to an inability to use wealth. They are suffering from a diabetes of wealth.

The sufferers from this diabetes have their own mode of life and belief: (1) Their sense of the ultimate is very strong. A man is born to marry and beget a son. The rest is immaterial. (2) They have developed a technique of living on the minimum. The hoarded cash is for the three nodes. (3) They are born to endure hardships in this life but will receive their reward in the next.

These are a few glimpses of the outlook which Sir John wants the educated Indians to change. This is essentially social reformers' work.

A medical man can undertake this work also as the 'social physician' of Sir Joseph's report. It will be necessary, however, to select him, lest he should be a wealth diabetic himself.

The selection will be by interview and mainly based on the interview. He will be derived from a respected section of the community and will be a knowledgeable physician and/or surgeon. He will be a bachelor and remain so during a probationary period. He will eat the food and speak the language of the community he is working in but will not bend his knee to its elders in every wish of theirs. He will be hardworking, sympathetic and polite, and he will make his profession a mission. -He will then succeed where civil administrators have failed for centuries, since Akbar's time if not Asoka's. His work will be blessed. Humanity makes the nearest approach to Deity in alleviating suffering.

S. D. S. G.

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Medical News

THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the D.T.M. Examination, Session 1945-46.

Passed

(Arranged in alphabetical order)

- Balkrishna Acharya, M.B., B.S. (Patna), Private Practitioner.
- Brindaban Chandra Bagchi, L.M.F. (Bengal), Medical Officer, Bengal Civil Protection Committee.
- Amal Kanti Banerjee, L.M.F. (Bengal), Assistant Medical Officer, Longsol Tea Estate, Assam.
- Prasun Kumar Banerji, M.B., B.S. (Patna), Private Practitioner.

- Sailesh Kumar Banerji, L.M.F. (Bengal), Private Practitioner.
- Anil Kumar Barat, M.B., B.S. (Patna), Private Practitioner.
- Jatindra Nath Batabyal, L.M.F. (Bengal), Assistant, Blood Bank, Pasteur Institute, Shillong.
- Subodh Chandra Bhadury, L.M.F. (Bengal), Pathologist, Atiabari Tea Estate, Jalpaiguri.
- Jagadindra Nath Bhattacharjee, L.M.F., L.T.M. (Bengal), Pathologist, Gopalpur Tea Estate, Jalpaiguri.
- Santosh Kumar Bhattacharya, M.B. (Cal.), Private Practitioner.
- Probodh Chandra Chail, M.B. (Cal.), Private Practitioner.
- Bimal Chandra Chatterjee, M.B. (Cal.), Private Practitioner.
- Sudhir Chandra Chatterjee, L.M.F. (Bengal), Private Practitioner.
- Madan Mohan Das, L.M.F. (Bengal), Assistant Clinical Pathologist, Chittaranjan Hospital, Calcutta.
- Monindra Nath Das, M.B. (Cal.), Private Practitioner.
- Kamalendu Dasgupta, L.M.F., L.T.M. (Bengal), Private Practitioner.
- Sukumar De, M.B. (Cal.), Private Practitioner.
- Harendra Lal Dhar, L.M.F. (Bengal), Private Practitioner.
- Chandra Madhab Dutta, M.B. (Cal.), Private Practitioner.
- Prithvi Raj Gambhir, L.M.S. (Punjab), Private Practitioner.
- Shiba Prasad Ghosal, M.B., B.S. (Patna), Private Practitioner.
- Nani Gopal Ghose, M.B. (Cal.), Private Practitioner.
- Grace Kathleen Gregory, M.B., B.S. (Rangoon), Private Practitioner.
- Amar Nath Gulati, L.M.P. (C. P.), L.M.F. (Cal.), Private Practitioner.
- Hala Lazarus Habil, L.C.P. & S. (Bom.), Assistant Medical Officer, Mission Hospital, Ratlam.
- Vaidyanatha Iravatham, L.M.F. (Mad.), D.L.Sc. (Madras Medical College), Honorary Pathologist, Government Hospital, Trichinopoly.
- Prabhu Diyal Khatri, L.M.P. (C. P.), L.T.M. (Bengal), Medical Officer, Sewa Santi Hospital, Muttra.
- Dasha Rathi Kheal, L.M.F. (Bengal), Assistant Medical Officer, Nya Sylee Tea Estate, Jalpaiguri.
- Albert George McClymont, M.B., Ch.B. (New Zealand), Surgeon Superintendent, British India Steam Navigation Co., Ltd., Calcutta.
- Jagadish Narayan Mehrotra, M.B., B.S. (Patna), Provincial Medical Service, Bihar.
- Mohamad Mazhar, M.B., B.S. (Patna), Assistant Medical Officer, Aden.
- Jatindranath Paul, L.M.F. (Bengal), Assistant Medical Officer, Malangi Tea Estate, Duars.
- Ram Sharan Prasad, M.B., B.S. (Patna), D.M.R.E. (Lucknow), Private Practitioner.
- Kanakamedala Ranga Rao, M.B., B.S. (Andhra), Medical Officer, A. G. T. Institute, Vuyyuru.
- Sewa Ram Sadana, M.B., B.S. (Punjab), Private Practitioner.
- Shyamapada Saha, M.B., B.S. (Patna), Private Practitioner.
- Gopal Chandra Sen, L.M.P. (Bengal), Medical Officer, District Board, Faridpur.
- Manindra Nath Sen, M.B. (Cal.), Private Practitioner.
- Nareschandra Sen, L.M.F. (Bengal), Clinical Pathologist, Calcutta Clinical Research Association, Ltd.
- Salil Chandra Sen, M.B. (Cal.), Private Practitioner.
- Chintamani Vishwanath Shevade, M.B., B.S. (Lucknow), Medical Officer in-charge, Victoria Hospital, Rewa.
- Harcharan Singh, M.B., B.S. (Punjab)—Awarded the 'Chuni Lal Bose' Gold Medal, 1946, Medical Officer of Health, Sargodha Municipality.
- Nageshwar Prasad Singh, L.M.P. (Patna), Medical Officer, Parsa Hospital, Bihar.
- Natasier Thiagarajan, D.M. & S. (Mad.), Sub-Assistant Surgeon, General Hospital, Pudukotah.
- Sudhanshu Kumar Upadhyay, M.B., D.P.H. (Cal.), Health Officer, Bhagalpur Municipality.

FOURTH CLINICAL MEETING OF THE
CALCUTTA SCHOOL OF TROPICAL MEDICINE
HELD ON TUESDAY, 15TH JANUARY, 1946

LIEUTENANT-COLONEL SIR J. B. HANCE, C.I.E., O.B.E., K.H.S., Director-General, Indian Medical Service, opened the meeting with a brief address.

Dr. John Lowe showed a case of amoebic liver abscess with almost complete absence of any general symptoms in a Mohammedan male, aged 50. The patient had dysentery eighteen months ago, and was treated with indigenous medicine with recovery. Six months ago, a swelling appeared on the right side in the liver region and steadily increased. There was some slight fever, but general symptoms were almost absent. The symptoms were all local, pain in the area of the swelling causing severe insomnia in recent weeks, and difficulty in eating apparently produced mechanically. The patient came to the hospital a fortnight ago, ambulant and afebrile. Clinical examination revealed an enormous swelling occupying the whole liver area and the upper right quadrant of the abdomen extending below the umbilicus. The swelling was intensely hard and tense. In the posterior axillary line at the back in about the 10th intercostal space there was much swelling, oedema of the tissues and fluctuation. Screening showed a markedly raised and completely immovable right dome of the diaphragm, the swelling pushing the mediastinum and the heart over to the left. The white cell count was 11,200 with 77 per cent polymorphs and 4 per cent eosinophils. Stool examination showed no protozoa. The intravenous hippuric acid test for liver function showed slight deficiency. There was no jaundice. Some defect in liver function was indicated by examination of blood proteins which with a normal total of 6.8 showed an albumin-globulin ratio 6 to 1 instead of 2 to 1. Treatment was instituted by emetine and aspiration, and during the next ten days, one gallon of pus was removed by aspiration, the aspiration being made at the site of fluctuation. The patient was apparently making a complete recovery, the liver was much smaller, and the diaphragm now moving.

Dr. G. Galstaun described a case of linitis plastica in a man aged 48, who two years and three months ago had both the clinical and x-ray signs of a lesser curvature ulcer. A definite ulcer niche was demonstrated in skiagrams of the stomach. This improved with Sippy diet and alkalies. In two years there was recurrence of epigastric pain and nausea, which became progressively worse. When examined in 4/42, the stomach had completely changed its character. From the hyposthenic long stomach in keeping with the patient's tall, slim build, it had become a small nearly transverse type of stomach, with no peristalsis and nevertheless rapid emptying—this with no palpable lump in the abdomen. The acid curve was, as originally, high throughout. No food could be retained. The patient died shortly after.

Dr. A. K. M. Abdul Wahed demonstrated with the help of a cinematographic film a case of paroxysms of violent rolling movements of the head, or of both head and trunk, during sleep, 3 or 4 times every night since the age of 4. The patient was a Hindu goldsmith, aged 18. The first paroxysm was the longest, and appeared within half an hour of sleep and lasted for about half an hour; the others lasted 5 to 10 minutes, the last one occurring during the early hours of the morning. The onset and the end of the spasm were sudden. With the spasm the respiratory sounds became very prominent, the inspiratory sound being heard when the head turned one side and the expiratory sounds when the head turned opposite. The movements were stereotyped and 30 to the minute. The paroxysms never occurred during waking hours. During the paroxysm, the patient is not only in deep sleep but probably in deep coma; he cannot be roused or brought to consciousness by pin-prick, or even by the application of naked flame to skin, or by resisting the movements. The limbs are flaccid; the jerks were present as far as can be elicited. The plantar responses

were neither flexor nor extensor. Towards the end of the fit the corneal reflex was absent, but returned within a few minutes of the cessation of the fit. The patient had no knowledge of the fits. The fit in itself was so violent that unless protected by soft pillows and bedding, there was danger of his face being smashed. The violence increased on resisting the movements. The patient was absolutely normal when awake. Narcolepsy, catalepsy, night terrors, hypersomnia, tics, spasmus nutans and epilepsy were discussed in diagnosis and Dr. Wahed suggested that it was a kind of epileptic fit which Russel Brain of London Hospital described as *epilepsis partialis continua* which occurs when the patient is awake.

Dr. R. N. Chaudhuri showed a case of multiple deficiency in a female with clinical manifestations of ariboflavinosis, scurvy and hypoproteinaemia. The peculiarity of her scurvy was the extensive hæmorrhagic rash on both extremities with no bleeding gums. She also had diarrhoea, absolute achlorhydria and dimorphic anaemia, and the x-ray pictures of the intestines appeared to be of the 'deficiency pattern'. The condition followed severe restriction of diet for diarrhoea and was cured by mixed diet with vitamin supplements and hæmatinics.

Dr. H. Rahman described and illustrated a case of amoebic ulceration of the skin of the anal region. A male, aged about 35, had been having attacks of dysentery for nine months, and for five months had been suffering from fever, and with ulceration near the anus for 15 days. The patient was weak and emaciated, and had an intermittent temperature up to 101°F. The spleen was markedly enlarged and the liver was enlarged and soft. There was no diarrhoea; the colon was not palpable, thickened or tender. The ulcer was of the size of a rupee, a little away from the anal orifice, and was very painful and extremely tender. The base was necrotic and there was a foul-smelling discharge. The margin was clear-cut and deeply undermined. No sign of inflammatory reaction was seen. Blood examination revealed anaemia; the white cell count was 3,100. Aldehyde and antimony tests were positive. Sternal puncture showed no parasites. Stool examination revealed ascaris and ancylostoma, but no *E. histolytica*. Treatment for kala-azar controlled the fever, but the ulcer went on spreading. Smear preparations made from the margin of the ulcer showed *E. histolytica*. Emetine hydrochloride 1 gr. daily for nine days was given with rapid improvement in the ulcer, and ultimate healing.

Dr. N. Gupta demonstrated a case of sub-acute bacterial endocarditis with complications. The patient, aged 30, was admitted to hospital for irregular and slow fever for 10 months, hemiplegia on the right side with aphasia for one month, and spasm over the left side of abdomen and in the upper part of the left thigh. His right hand was amputated 3 years ago as a result of injuries sustained in a skirmish; a year ago he had an attack of palpitation for which he was laid down for some time but there was no history of syphilis or rheumatic fever. A month ago, he became unconscious and remained so for two days and the present condition started since then. Physical examination revealed anaemia, clubbing of fingers and carotid pulsation; the pulse was collapsing, but regular in rhythm; blood pressure 110/40; heart—apical impulse, 6th left intercostal space 1 inch lateral to the mid-clavicular line—systolic murmur conducting towards axilla and diastolic murmur conducting along the left side of the sternum; liver and spleen soft and enlarged; all jerks exaggerated on the right side, plantar reflex extensor and abdominal reflex absent on right side. The blood count showed slight leucocytosis with relative increase of neutrophils. The blood culture was repeatedly negative. W.R. doubtful. Glucose tolerance test and urine examinations were normal. Nothing abnormal was detected in skiagrams of legs and feet. The patient complained of burning sensation and pain in the left leg particularly on the tips of the toes, and within two days discoloration appeared over the distant part of the left foot. There was a crippling

pain particularly in the calf of the left leg with a sense of rigidity and constriction, and pulsation of dorsalis pedis arteries and posterior tibial arteries could not be felt on both the legs. Trophic ulcers appeared a few days later, and dry gangrene set in at the tips of the toes. Potassium iodide in gradually increasing doses from 15 to 90 grains thrice daily was given. After a fortnight plantar reflex was flexor and the abdominal reflex became normal on the right side. Pain and cramps disappeared within three weeks. Application of heat, or heat and cold, had no effect on the arteries and the pulsation did not appear. On allowing the legs to hang for some time, the coloration disappeared slightly but no pulsation could be felt. The history of fever with palpitation of the heart, repeated attacks of fever with slow rise for more than a year, with anæmia and clubbing of the fingers, systolic murmur at the mitral area and diastolic murmur at the aortic area, and enlargement of the spleen all point to a diagnosis of sub-acute bacterial endocarditis. The hemiplegia with aphasia, as also the leg and the foot condition were embolic phenomena. Whether this unusual condition of embolus on both legs was due to angitis obliterans or syphilitic infection as was suggested by the good results obtained with large doses of potassium iodide was discussed.

Demonstrations were also given by the following authorities on the subjects mentioned: Lieutenant-Colonel J. A. Shorten on eversion of the diaphragm, Major J. B. Fisher on intra-uterine tumour, Dr. P. C. Das on evolution of midwifery forceps, A. K. M. Abdul Wahed on herpes, and Dr. S. Bhattacharjee on hydatid cyst with multiple infestation.

FIFTH CLINICAL MEETING OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE HELD ON TUESDAY, 5TH FEBRUARY, 1946

At the fifth meeting, Dr. D. G. Davey gave an account of the recent researches with antimalarial drugs in bird malaria, especially paludrine, M 4888.

Dr. N. Gupta described a case of (?) malignant tumour of the suprarenal cortex in a boy of 16 years. The patient was admitted to hospital for gradual enlargement of the breasts, beginning with a slight inflammation and pain on both breasts and persisting for 6 months, while at the same time the penis and testes were diminishing in size. Before this period he had behaved as a normal young man with sexual attraction, penile erection and pollution. He has now lost all sexual feelings and penile erection; only a slight tendency to turgidity was left. There was no pollution and no feeling of pain on pressure on the testes. The penis measured $1\frac{1}{2}$ inches and the testes atrophied. The breasts were well-developed female breasts with enlargement of glandular tissue giving out a slight serous discharge on pressure. The nipples were large and pigmented. The face was feminine in appearance, smooth and without hairs although he reported that he used to shave a year before. The distribution of hairs was getting scared and feminine in character in the axillæ and pubis. The voice was also feminine. Besides the pigmentation over the nipple and areola, there was also pigmentation over the linea alba. The lower abdomen had assumed a feminine character with a sharp upper horizontal border. The right renal angle was very tender on pressure. Liver and spleen were not palpable and there was no evidence of any infiltration anywhere. Friedman's test was negative. Skiagram of the skull and the epiphyseal joints of the long bones were reported normal.

Dr. K. Hossain discussed a case of aneurysm of the aorta. A Hindu male, aged about 35 years, while visiting a prostitute, fell down unconscious on the bed. He was removed to the verandah where he died. No marks of injury or violence could be detected on the dead body. Post-mortem findings—a fairly nourished subject—rigor mortis present, eyes partly opened, pupils dilated and equal, conjunctivæ suffused—finger

nails cyanosed—heart 12 oz., enlarged, right coronary artery sclerosed, both sides containing blood—aneurysm at the beginning of the aorta which had burst into the pericardial sac, ascending part of the arch markedly atheromatous—pericardial cavity contained 13 oz. clotted and 2 oz. fluid blood—both lungs congested and with pleural adhesions—right pleural cavity contained 4 oz. serous fluid and left cavity 2 oz.—stomach, liver, kidneys and brain congested—spleen slightly enlarged—alcohol found in the stomach and traces in the liver and kidneys. The age, sex and habits of the dead man, the site and type of the aneurysm and enlargement of the heart with coronary sclerosis, all suggested that the aneurysm of the aorta in this case was due to syphilitic meaoertitis causing weakening of the arterial wall.

Dr. D. Panja showed a case of epidermolysis bullosa in a Hindu male, aged 22 years. The disease is hereditary as well as congenital. It is a very rare disease characterized by the appearance of blisters at points of friction or injury starting from infancy or childhood and persisting all through life. The blisters heal up rapidly leaving pigmented or depigmented scar. The lesions appear normally on parts of the skin exposed to injury, e.g. hands, back of knuckles and phalanges, elbows and knees. In many cases there is a partial or complete absence of dystrophy of nails and in this case here there is complete absence of nails. The exact pathogenesis is not understood but it has been regarded as the result of three factors namely: (1) a peculiar congenital want of cohesion in the prickle cells, in consequence of which an excess of fluid in the inter-epithelial lymphatic spaces readily leads to the separation of the cells and the formation of a bleb, (2) an excessive instability of the vasomotor control of the cutaneous blood vessels, in consequence of which rapid dilatation and excessive transudation of serum readily occur, and (3) a diminution or absence of the elastic tissue.

Dr. M. Catchatoor described a case of retained placenta treated on conservative lines. A Hindu primipara, aged 25 years, was admitted to hospital with a history of having delivered a still-born female child the night before. She had had severe post-partum hæmorrhage and the placenta had not been expelled. She had not passed either stool or urine since the delivery. On examination the patient looked extremely ill and anæmic; pulse 138 per minute, volume and tension fair; respiration hurried; blood pressure 108/60. The abdomen was very distended, and the bladder was masking the fundus of the uterus. Visible peristalsis was present in the upper half of the abdomen. There was a very thick black and offensive discharge per vagina, and on removing the degenerate clots, the cord and membranes were seen protruding. The perineum was markedly œdematous and was torn up to the rectum. On catheterizing the bladder the fundus of the uterus was found to be at the level of the umbilicus. Foul-smelling gas and degenerate blood clots escaped on massaging the fundus. Blood examination showed rbc 1.89 million per c.mm., hæmoglobin 38 per cent (5.25 gm.), and white cells 27,000 per c.mm. The urine was sterile on culture and the W.R. was negative. Manual removal of the placenta was not considered suitable under existing conditions of shock and sepsis. Glucose saline 500 c.c. was given by intravenous drip method pending the arrival of 250 c.c. of suitable blood. Penicillin 15,000 units were given intramuscularly for four days to a total of 400,000 units. Locally a low pressure douche was given. On the third day two inches of the cord and a portion of the sloughing membranes were cut off. The involution was charted from the eighth day of admission and progressed steadily and normally. The local condition began to improve, but the patient still ran a temperature of 99 to 100°F., the pulse rate remained high, and the blood picture was the same. A second blood transfusion was given on the 20th day. There was an immediate sharp rise of temperature which came down to normal in a few hours. After that the patient remained afebrile and the pulse rate became regular and steady. The

uterus became normal in size, antverted and freely movable, the cervix healthy and free from discharge. The blood picture also improved.

Captain E. J. Somerset gave a demonstration of xeroderma pigmentosa.

MEDICAL COUNCIL OF INDIA

THE Medical Council of India met for its Twenty-fourth Session at New Delhi on the 23rd March, 1946. The President, Dr. Abraham S. Erulkar, M.D., was in the chair.

The president in his address mentioned, with regret, the resignation of Sir James Hance from the Council and referred to his services to the Council. He welcomes General Hay to the Council in the vacancy caused by the resignation of Sir James Hance and also Dr. Sen Gupta representing the medical graduates of Central Provinces and Berar, and Colonel L. K. Ledger, representing the Government of Central Provinces and Berar. He then gave a brief summary of the activities of the Council since 1936, and made an appeal to the representatives of the universities to use their influence to obtain the concessions recommended by the Council to be granted to the licentiates to enable them to take M.B., B.S. degrees. In connection with obtaining recognition of Indian degrees abroad, the president stated that though the Council has established truly reciprocal relations with the General Medical Council as far as most of the universities of schedule I are concerned, the General Medical Council recognizes the degrees of the Patna University when granted on or before 11th May, 1935, and those of the Calcutta University when granted on or before the 16th October, 1936, only. Andhra University degrees are not recognized at all. Regarding other countries, the position is more unsatisfactory. Even in India itself, our graduates cannot practise in French India whilst practitioners with French India qualifications can do so in British India. Among foreign countries, only three—Burma, Malta and New Zealand—are under direct reciprocity. The president also pointed out that it is now twelve years since the universities were first inspected and that a fresh inspection is overdue, more particularly as new medical colleges are being added.

The Council elected Dr. K. S. Ray as its Vice-President, Rai Bahadur Dr. B. N. Vyas, General Hay and Colonel Bharucha were elected to be members of the Executive Committee.

Amongst the several important matters discussed by the Council, the question of the establishment of an All-India Medical Register which has been agitating the Indian Medical World for a considerable time was one. The Council had discussed this question at several of its previous sessions and had made certain recommendations which have been considered by the Provincial Governments as well as by the Provincial Medical Councils. During this session, the Council gave further consideration to the various points raised by these authorities. As the result of these deliberations, the Council has made certain additions to their previous recommendations, and the All-India Register will now include all persons holding qualifications on the schedules of the Indian Medical Council Act and those practising modern system of scientific medicine in British India and possess qualifications granted by Licensing Bodies in British India together with those Indian Nationals, who hold foreign qualifications not recognized by the Indian Medical Council but recognized and registered by Provincial Medical Councils. These will be divided into three groups and this distinction will remain till such date when there is one minimum standard of medical qualifications established throughout the country. The Council were of the considered view that this was not only a decided advance on the previous position but under the limitations of the existing conditions had the merit of meeting all the various points of view in the country.

The Council also deliberated on the question of the recognition of the medical degree granted by the Agra

University. Their Inspectors had already reported on the courses of instruction as well as the various examinations held by the University. The University authorities' observations on the reports of these Inspectors were before the Council. The Council has now appointed two of its members to act as Visitors and to report to the Council as to how far the recommendations by their Inspectors have been carried out.

The question of the consideration of the Bhoze Committee Report has been referred to the Executive Committee, a special session of which is being held shortly for the purpose.

The next meeting of the Council has been fixed for the 19th of October, 1946.

AUSTRALIAN MATERNITY HOSPITALS

THE King George V Memorial Hospital, Sydney, is a fine example of the new type of institutions now being built to safeguard maternal and infant health in Australia.

Expert care and health teaching is given to all expectant mothers irrespective of income from the time the mother first realizes she is pregnant until her baby has made a good start in life.

Outstanding features of the hospital include the separation of maternity and gynaecological patients; antenatal, postnatal and dental clinics; an emergency delivery room adjoining the ambulance entrance; sterile water throughout the hospital. There are 6 labour waiting rooms with a coloured light 'No admission' system and a sliding panel through which the hospital staff can watch progress without disturbing the mother. After delivery in one of the two well-equipped delivery rooms, the baby is taken to one of the two nurseries holding up to 50 babies where he is washed and weighed 6 hours after birth. Visitors can see the babies through glass partitions and only the nurse, gowned and masked, is allowed in the nursery.

Covering the whole of the ceiling of the operation theatres is a vault of stainless steel which acts as a reflector to the water-cooled projection light outside the room. Students and nurses sit above the vault and watch the operation through apertures in the vault. They ask questions or hear the surgeon's explanations by means of a speech amplifying system. The Hospital Library cost Rs. 42,10,000.

THE PRACTITIONER

SIR HENEAGE OGILVIE, K.B.E., M.D., M.Ch., F.R.C.S., has been appointed Editor of *The Practitioner* in succession to Dr. Alan Moncrieff, M.D., F.R.C.P., who has resigned on his appointment to the Nuffield Professorship of Child Health at The University of London. Sir H. Ogilvie, who received his knighthood in the New Year Honours List for distinguished services during the war, is Surgeon to Guy's Hospital, a Vice-President of the Royal College of Surgeons, Honorary Major-General and Consultant Surgeon to the British Army.

Professor Moncrieff has been Senior Editor of *The Practitioner* since 1943 when he succeeded the late Sir Humphry Rolleston, Bt. Dr. William A. R. Thomson who joined *The Practitioner* in 1944 will continue as Associate Editor.

RECENT WORK ON TRYPANOSOMIASIS AND TSETSE FLIES

In response to requests for information, the Bureau of Hygiene and Tropical Diseases, London, has published a monograph, 'A survey of recent work on trypanosomiasis and tsetse flies' (price, 7s. 6d. net), based on reports and papers published since 1931. It gives a description of the geographical distribution of sleeping sickness, protozoological research, chemotherapy, biology of tsetse flies and control of the disease. The survey has been compiled by Charles Wilcock, J. F. Corson and R. L. Sheppard of the Bureau.

Public Health Section

STUDIES IN THE HEALTH PROBLEMS
OF A RURAL COMMUNITY IN
WESTERN BENGAL

Part I. Population Problems*

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and

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Introduction

SINGUR Health Centre Area comprising of 32 square miles, situated 21 miles north-west of Calcutta and consisting of 4 Unions, has been organized as a rural practice-field for the All-India Institute of Hygiene and Public Health, Calcutta. A general health survey of this area was conducted with the following objects:—

1. To obtain an integrated picture of the health conditions of the population, and of some of the factors likely to influence the state of community health.

2. To crystallize the main health problems of the community and to determine if possible their relative importance, thus helping in the formation of a progressive and well-balanced public health policy for better health protection and health building.

3. To serve as the base for assessing the extent of progress that might be achieved as a result of specific health measures by carrying out periodical surveys of special types.

4. To collect material and obtain a deeper appreciation of the health problems for purposes of teaching.

The survey was carried out on a random sample of 1,197 families consisting of 7,058 individuals out of a population of 11,900 families with 63,000 members. A report enclosing a general description of the methods employed and of the main findings has been submitted to the government.†

It is now intended to present further analysis and more detailed discussion of some of the public health problems based on the data collected during the survey in separate communications. It is recognized that a discussion of population problems based on a study of a small area like this will be subject to serious limitations. However, some information has been obtained which is not generally available under Indian conditions and which may be of wider interest.

* Read at the Indian Science Congress held in Bangalore.

† The report will be published shortly. It may then be obtained from the Director, All-India Institute of Hygiene and Public Health.

Age and sex constitution

The age and sex constitution of the sample population of the area is presented in figure 1. The maximum and minimum values at 5 per cent level, arising out of sampling error, are also

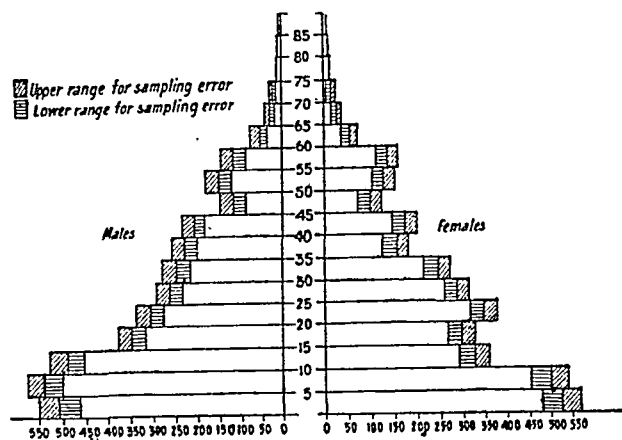


Fig. 1.—Age pyramid for Singur, 1944 (sampled population).

shown. It will be observed that the pyramid is more or less regular in shape. For purposes of comparison, the pyramid of age and sex constitution of Bengal according to 1941 census is given in figure 2. The latter antedates the former by 3 years, and consequently, a

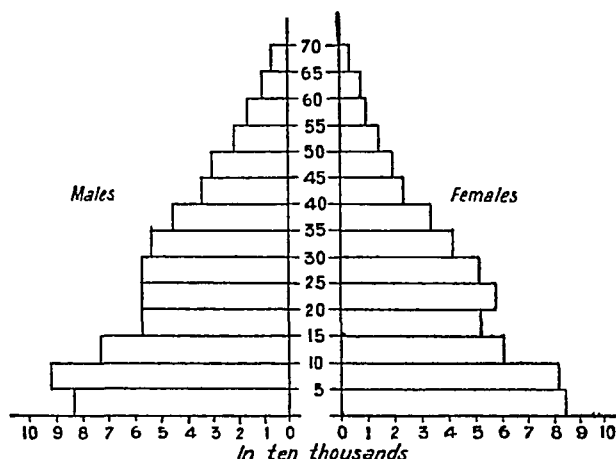


Fig. 2.—Age pyramid for Bengal up to 70 years of age (sampled population according to 1941 census).

strict comparison of the various steps of the pyramids cannot be made. However, in general, the two pyramids closely resemble each other. The first irregularity in the pyramid for Singur, is, that instead of being the largest, the bar representing the number of males in the 0-5 age group is smaller than that for the 5-10 age period. Strangely enough, the same feature may be observed even with a greater difference in the pyramid for Bengal. On the female side also, the two pyramids in these age periods, are

similar, although the Singur data are somewhat more irregular than those of Bengal. The reason for these irregularities may be found in the famine conditions prevailing in Singur in 1943 and the particularly high incidence of smallpox during the years 1940-41 in Bengal. Subsequent irregularities in childhood and early adolescence in Singur may be accounted for by fluctuating birth rate and infant mortality rate as deduced from the available data for these rates for Bengal with more or less corresponding fluctuations in the pyramid. The undue contraction of the Singur pyramid for both sexes, at age period 45-50, is probably due to famine conditions prevailing in 1897. However, the pyramid for Bengal does not exhibit this irregularity. Another point which may be noticed is the relatively smaller number of females at each period both in Singur and in Bengal. In contrast to these data one may see figures 3

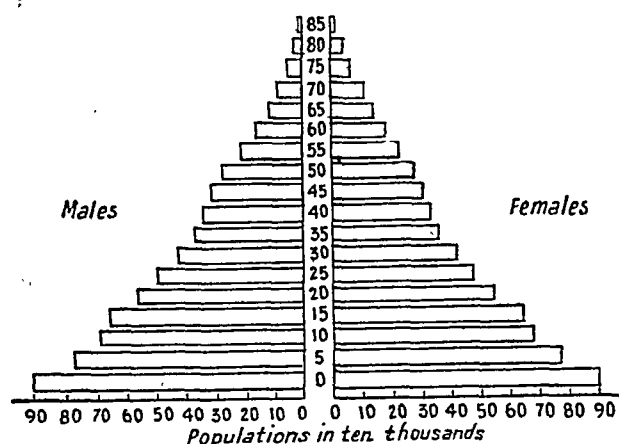


Fig. 3.—Age pyramid for Japan, 1930.

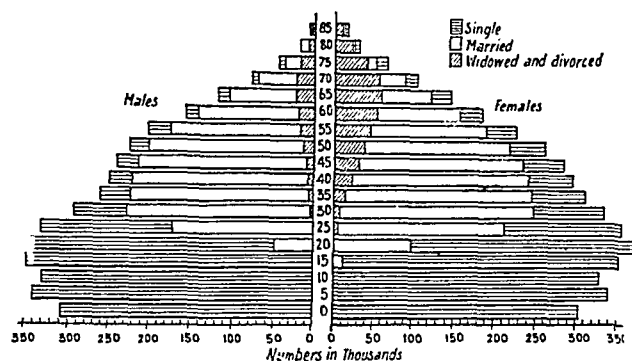


Fig. 4.—Civil condition of census population, England and Wales, 1931.

and 4 in which the age and sex pyramids for Japan and England and Wales are presented. In general shape, the Japanese pyramid is intermediate between the British and Indian figures, and, like the latter, exhibits a smaller number of females for the corresponding age groups. The Japanese pyramid is more regular in shape than the others; the English pyramid, on the other hand, presents quite a different appearance. The base is small, but the bars increase in length, till the age of 15-20 for

males and 20-25 for females. Hereafter, they decrease. One may therefore infer that birth rate has progressively decreased year by year. Another important feature is that the decrease in numbers in quinquennial periods at advanced ages is small, giving a bulging or dome-shaped appearance to the pyramid, which suggests a higher expectation of life.

Civil state

There is a marked correspondence between the pyramids of Singur and Bengal (see figures 5 and 6). The principal features are early marriage particularly of the females and large

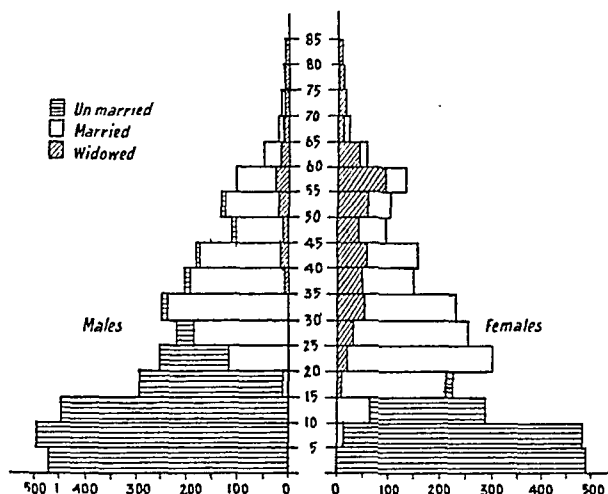


Fig. 5.—Civil condition of sampled population, Singur, 1944.

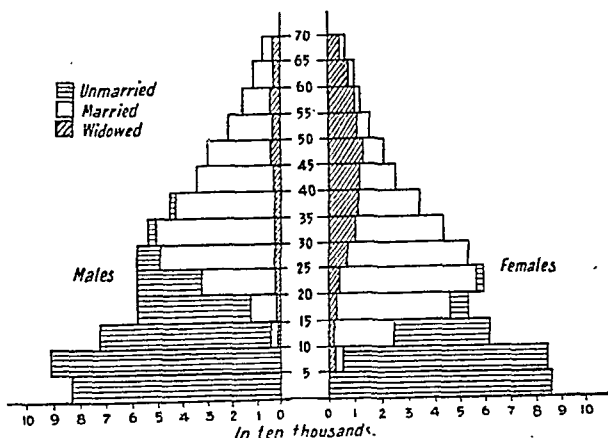


Fig. 6.—Civil condition of sampled population, Bengal, 1941 (up to 70 years).

numbers of widows starting early in life. As may be expected, the difference between the ages of husband and of wife suggested by these figures is approximately 5 years. The universality of marriage in the Indian data sharply contrasts with the corresponding British data in which incidence of broken homes is relatively less common.

Age at marriage.—Reference has already been made to early marriages particularly among the females in Singur and in Bengal. The average

age at marriage for women at Singur is 12 years, whereas Sarda Act prescribes 14 as the minimum marriageable age. However, as will be seen from table I, there is a gradual but steady trend towards the postponement of marriage, the average age at marriage having advanced by 1.5 years in the course of a generation. Whether or not in the near future this desirable trend will be accelerated it is difficult to say. The present experience shows that the average age at marriage does not materially vary in the three economic groups into which the population has been divided, but it does so amongst the literates and the illiterates, the average age for the former being 11.3 and for the latter 12.6. The data do not provide analysis for different communities, but the population is predominantly Hindu and fairly homogeneous and it is not likely that much light may be thrown on the problem by such analysis. Taking everything into consideration, it seems likely that advancement in the education of women is likely to bring about the desirable reform in raising the age of girls at marriage with its attendant advantages socially, economically and in matters of health of mother and child. However, the process may be further accelerated by a well-planned and organized propaganda directed towards this reform. It may be added here that any scheme to propagate these ideas should at the same time provide against the danger of illegitimate pregnancies which may create new social and health problems.

Births

As a direct result of early marriage of Indian girls, first births are confined to young mothers, under 30 years, in marked contrast to the American experience, especially that relating to native white people, amongst whom first births in appreciable proportion continue till the end of the reproductive period. This tendency was more marked in 1930 than in 1920 among white women, but not so among the coloured people (*vide* table II). A factor of greater importance which results in postponement of the first delivery to advanced age is the practice of birth control, which is practically non-existent in Singur.

The crude birth rate in Singur for 1943 was 42 and corrected birth rate 44 per mille, as against 34 for Bengal and 33 for India in 1940. Thus, the birth rate in Singur in the year under report was considerably higher than in Bengal and India in recent years. The British and the American figures were much lower, being 14 and 17 in 1937. Only three abortions and 11 still-births were discovered in the course of the survey among the sample population, giving abortion and still-birth rates of 1 per cent \pm 0.5 and 3.7 per cent \pm 1.0 respectively. These rates are lower than the American rates, particularly the abortion rate which according to Pearl (1939) varies from 12 to 21, depending upon the number of pregnancies experienced by women. In British experience (Burns, 1942) the abortion rate rises from 1 per cent in the primipara to 18 per cent in the 12th pregnancy

TABLE I
Age at marriage for women of various age groups at Singur

Quinquennial age groups

		-20	-25	-30	-35	-40	-45	-50	-55	55 or over
Number of women ..		152	317	266	243	152	166	91	107	265
Average age at marriage ..		12.0	11.8	11.6	11.5	11.1	11.1	10.9	10.8	10.5

TABLE II
Percentages of living first births to all living births at different age periods

Age	SINGUR	AMERICA					
	Percentage of first birth	Native white		Foreign born white		Coloured	
		1930	1920	1930	1920	1930	1920
10-15	100.0	99.6	98.5	100.0	95.2	99.7	98.0
15-20	73.1	79.3	82.1	78.5	76.7	72.5	77.2
-25	15.7	46.0	48.4	51.0	41.3	29.3	38.5
-30	3.1	24.3	24.8	28.0	16.6	10.4	12.9
-35	0.0	12.3	12.1	12.2	7.0	5.2	6.6
-40	0.0	6.4	6.1	5.3	3.6	3.0	3.2
-45	0.0	3.7	3.3	2.6	2.3	1.8	2.1
-50	0.0	2.7	1.9	1.7	0.6	1.5	1.6
-55	0.0	9.2	7.7	0.0	0.0	2.4	3.3

and to as much as 40 per cent in the 13th pregnancy. In the present series only 22 per cent of the mothers were primiparas, and women with a large number of pregnancies were not uncommon. Hence the difference in the order of pregnancies in the two countries cannot furnish the explanation.

It is interesting to note that the percentage of women negative for Rh factor who would mostly contribute to abortion and still-births, as found by Greval and Roy Chowdhury (1943) in Calcutta is about the same (10 per cent) as found by Wiener (1945) and others in America. The incidence of syphilis in the rural population is not definitely known, but it is likely to be low. Against this, there is the high incidence of malaria and other acute diseases which may contribute to loss of life during gestation.

Thus we are not in a position to offer any satisfactory explanation of low abortion rate at Singur, but it may be mentioned that the data collected at Maternity and Child Welfare centres in Calcutta also show a low rate (2.5) according to an unpublished report of L. S. Ghosh and C. Chandrasekar. At any rate, it is important to remember this fact in the assessment of antenatal service.

TABLE III

Still-birth rate (1943) at Singur according to age of mothers

Age of mothers	Number of still-births	Total number of live births	Percentage of still-births
-15	0	1	0
-20	4	56	7
-25	4	93	4
-30	2	68	3
-35	1	46	2
-40	0	19	0
-45	0	9	0
-50	0	2	0
-55	0	0	0

As will be seen from the table III, the proportion of still-births to total births is somewhat higher in young mothers under 20 years than amongst those above 20 years. However, as will be observed from table IV, this difference may arise from the high incidence of still-births amongst primiparas as compared with multiparas and as we have already seen (table II) about two-thirds of the mothers below 20 years of age are primiparas.

TABLE IV

Incidence of still-births according to order of pregnancy at Singur in 1943

Order of pregnancy	Number of still-births	Total number of births	Percentage of still-births
1	7	63	11
2	1	49	2
3	2	49	4
4	0	32	0
5	0	32	0
6	0	21	0
7	1	17	6
8	0	13	0
9	0	10	0
10	0	8	0
and over.			

Twin-births were rare; in fact, only one such case came to our notice among 307 births. According to Crew (1927) the expected number of twin-births would be 4 for the above numbers of births.

Seasonal distribution of conception

Table V shows the month in which conception took place, as calculated from the month of gestation in case of pregnant women and the date of birth of infants born within a year from the date of survey. The average number of conceptions per month is 28 and a perusal of the table V shows that, beginning from November, conceptions become more numerous during the winter, and remain so till the following March. During the summer and the rains the number of conceptions is relatively small.

From an analysis of the data given in the reports of the Director of Public Health, Bengal, for years 1931-1940, it would appear that the months of maximum rate of conception are January and February and of the lowest October and November. According to the present data, the conception rate is highest a little earlier than the time suggested by the Bengal data. The lowest rate also occurs a month earlier.

Mukerjee (1938) suggests malaria as the principal reason for the lower incidence of conceptions at certain time of the year. Since the malaria morbidity curve reaches its maximum in Singur by September, the results obtained here are consistent with Mukerjee's hypothesis.

TABLE V

Seasonal distribution of conceptions in the sample population

Number of conceptions estimated from :	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Survey of pregnant women ..	9	7	6	3	3	5	5	10	5	4	7	9
Survey of births ..	35	23	33	15	10	20	22	12	12	18	25	38

TABLE VI
General fertility rates for Singur and certain countries*

Country	Year	Percentage of women of child-bearing age to total population	General fertility rate
Singur area ..	1943	20.40	213.2
England and Wales ..	1930/2	28.01	56.43
Scotland ..	1930/2	26.97	70.88
Australia (excluding aborigines).	1932/4	26.27	63.49
New Zealand (excluding Maoris).	1925/7	26.40	79.37
Canada (including Yukon and N.W. territories).	1930/2	24.77	93.42
S. Africa (Europeans only).	1925/7	25.49	102.68
United States (all races; areas excluding Texas and S. Dakota).	1929/31	26.55	70.04
Sweden ..	1932/4	26.94	51.86
Germany (excluding Saar).	1932/4	27.98	57.64
France ..	1930/2	26.48	67.37
Italy ..	1930/2	26.40	95.35
Ukraine ..	1926/7	26.49	155.57
Japan ..	1929/31	23.55	137.59

* Quoted from 'Population and Fertility' by D. V. Glass and C. P. Blocker (1938).

TABLE VII
Specific fertility rates per 1,000 married women per annum at Singur

	Age groups							
	-15	-20	-25	-30	-35	-40	-45	-50
Calculated from termination histories.	20	116	260	300	260	100	20	20
Calculated from births in 1943.	12	218	294	268	186	126	54	22

General fertility

Apart from fecundity, the birth rate varies with a number of factors, for example, the percentage of women of child-bearing age in the population, the age at marriage, the percentage of widows, the percentage of women that marry, and the use of contraceptives. The Indian population differs from the population of other countries in all the factors mentioned above; the proportion of women in the child-bearing period is the lowest of all the civilized countries, while the marriage is universal and the marriage age is low. So far as we know, contraceptives are not used. In the circumstances, it is not surprising that the general fertility rate is highest (see table VI) compared with other

countries, being 213 as against 51 for England, 56 for Sweden and 58 for Germany. Ukraine which comes next highest has a rate of 156 only. The age of highest fertility is between 20 and 30 (see table VII). In other countries, it is at least 5 years later. The net reproduction rate is comparatively moderate as may be seen from table VIII. It is evident that a high mortality rate prevents over-replacement of mothers, and the rate of growth of the population is thus reduced. However, the percentage of the married women is high, and the duration of married life, in its most reproductive period, is larger. However, a check is furnished by the custom that widows do not generally remarry and by the fact that the percentage of widows is high. Taking into consideration the age specific fertility for women and the age distribution at widowhood it is estimated that the reduction in the growth of population due to this cause amounts to 15 per cent. This is a high figure which must necessarily affect the net reproduction rate and the rate of growth of population.

TABLE VIII

Gross and net reproduction rates for Singur (1943) and certain other countries*

Country	Year	Gross reproduction rate per 1,000 women	Year	Net reproduction rate
Singur area ..	1943	2,940	1943	1.13
Germany ..	1934	983	1936	0.90
France ..	1930-31	1,117	1936	0.88
Italy ..	1935-37	1,424	1933	1.18
United Kingdom of England and Wales.	1931	933	1934-36	0.76
Ukraine ..	1926-27	2,507	1926-27	1.68
United States of America.	1929-31	1,108	1936	0.95
Japan ..	1930	2,295	1930	1.57

* Quoted from International Vital Statistics published by the Vital Statistics Bureau of the Census—Washington.

Sex ratio

The male population is 52 per cent; thus the males outnumber the females. However, the mortality rates among males is higher than amongst the females in all age groups except the age groups 10-15, 35-40 and 45-50. Since the Singur population is not influenced by immigration it would be expected that the sex ratio at birth would be greatly in favour of the males, and it is known that the males outnumber the females generally. However, it is not so for 1943 according to the information collected in the survey; the females outnumber the males at birth, but the difference is not significant, being less than twice the standard error due to sampling.

The inter-relation between the growth of population, poverty and health has exercised the minds of many thinking people in this country. It is recognized that these problems involve much complexity and do not admit of a fruitful discussion without a full comprehension of historical, political, psychological, sociological and economic background, and also possibilities of scientific development in near future. However, it should be possible to present certain aspects of the problem from the viewpoint of a student of public health, even with the consciousness of the limitations which such treatment imposes. Amongst the factors involved in determining the material production of a community such as richness of natural resources, capital and technical skill, state backing and urbanization, there are certain human factors in which our present interest lies, *viz*, the proportion of 'active' population as against the population to be supported and the physical quality of the population and nature of burdens devolving upon the 'active' population which arise from ill health.

of 'active' women. For purposes of discussion we may reduce the upper limit of the period of active work to 55 instead of 60. The percentage of the population in the age period 15-55 in Bengal does not compare unfavourably with that of India, and still the percentage of 'actives' in Bengal is markedly lower than in India, the percentage of 'actives' in both sexes combined being the same as that of the females for India. The difference will be greater if Bengal is excluded from the all-India figures. The lower percentage of 'actives' in Bengal is referable to both male and female, but is specially marked in females, amongst whom only 7.5 per cent are 'actives' against 28 per cent for whole of India. In Singur the percentage of the population included in the age period 15-55 is less than that of the province or of the country, but the percentage of males employed is very nearly the same as in India, while the females employed constitute only a very small percentage (3 per cent). The total 'actives' form 31 per cent, which is somewhat higher than Bengal, in spite of the unfavourable age constitution.

TABLE IX

Percentage of economically 'active' people in various populations

	Singur, 1944	Bengal, 1931	India, 1931	France	Russia	Germany	Italy	England and Wales	Japan	U.S.A.	Canada
Percentage of active people in total popu- lation.	31.0	28.8	44.0	56.0	51.7	51.3	47.3	45.3	42.6	39.6	36.1
Percentage of active males.	57.0	48.1	58.0
Percentage of active females.	3.0	7.9	28.0

Proportion of 'active' population

1941 census for India does not give the proportion of 'active' population as against the supported, but from the previous three censuses it would appear that the proportion of the 'active' has progressively decreased during 20 years. Thus, the percentage of 'active' according to censuses of 1911, 1921 and 1931 were 47, 46 and 44 respectively. The reasons for this are not clear. Whether and to what extent the world war II influenced this figure is not known. But it would be reasonable to assume that sheer need and the facility for work must have heavily drawn upon the hitherto supported people into the category of the 'actives' and the percentage of 'actives' must have undergone a considerable increase by 1943. Even before the war, the percentage of 'actives' in India compared favourably with other countries, in spite of certain handicaps arising from age and sex constitution of the population structure as may be seen from table IX. A comparison between Bengal and India presents marked contrast, especially in regard to the percentage

However, Singur data refer to a period of unusual stress, when people were pressed by necessity and circumstances to take up as much work as possible. In Singur obviously males younger or older than the age periods included in the discussion have to work. In India also during the period of depression children and old people were normally engaged in gainful occupation. It is however remarkable that in Singur even the period of stress did not bring out women to take up occupations to supplement the family income. On the other hand, less than 1 per cent of males between 15 and 55 were out of employment. Only in one instance was ill health given as the reason for unemployment. However, the contribution of ill health to loss of working time and efficiency is not inconsiderable, because at any time 10.5 per cent of wage-earners were unwell, and either could not work at all or could not contribute full quota of their work. Over 3 per cent were acutely or chronically ill, and if they were carrying on the work under pressing necessity, they could only do so at the expense of their health and probably

at the risk of the health of their co-workers. On an average, nearly 38 per cent of the wage-earners have had one or more sickness during the year. Each sick person lost on an average 52 days, and considering the population as a whole, each adult on an average lost 20 days in the year. The working capacity of the population and probably the mental and physical efficiency could be considerably increased or improved upon if the amount of sickness could be reduced or recovery be expedited through specific and non-specific measures. By this means, the constitution of the population would also be indirectly influenced, because mortality in childhood and the early adult life could be lessened and the effective working age period prolonged. In short, it may be stated that for various reasons which may not be enumerated here, the male population is evidently under duress so that not only children and adults have to work for a living but also the sick persons cannot get sufficient rest for recuperation. Apart from other important remedies in the economic field, encouragement to women to take up gainful occupation should provide some relief to the hard-working male if he is to provide the bare necessities of life without unduly injuring his health. The higher morbidity and mortality among the males may be due to this circumstance.

It is difficult to say how the growth of the population is affecting the problem of standard of living and employment, but from the limited information available from our data, it would appear that even without the practice of contraceptive, the rate of population growth is only moderate, the net reproduction rate being only 1.13.

Summary

A general health survey of a rural community in western Bengal has been carried out, and certain aspects of the population problem are reported here. Special interest attaches to this problem in Bengal because the Province is the most densely populated in India. The density of population in Singur Area is 1,900 per square mile. The community studied is reasonably representative of Bengal with regard to age and sex constitution as well as civil condition. The birth rate is high. Conceptions take place more frequently in winter than in summer. The gross reproduction rate is 2.94 and the net reproduction rate is 1.13. The high birth rate due to universality of marriage which takes place at an early age and the incidence of highest fertility in young women of 20-25 combined with a high rate of mortality at early age periods explain the difference between the two reproduction rates. There is a high incidence of widowhood which reduces the rate of growth of population to the extent of 15 per cent. Still-birth and abortion rates are low as compared with foreign countries, and multiple births are rare. In keeping with conditions in the rest of

Bengal, the percentage of people who are economically active is markedly lower than the rest of India. This is mainly due to the women not being engaged in gainful occupation.

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THE STATE OF NUTRITION AND PHYSICAL DEVELOPMENT OF SCHOOL CHILDREN IN HYDERABAD STATE *

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THE nutrition section of the Public Health Department of H. E. H. the Nizam's Dominions undertook to do nutrition surveys and to ascertain the dietary habits, existence of deficiency diseases and physical development of the people. In this paper an attempt is made to find out standards of nutritional status and to ascertain the incidence of malnutrition and deficiency diseases amongst children.

The field of study covers some 100 surveys involving over 17,000 school children belonging to about 1,500 families of Muslims, Telangees, Marathas and Kanarees at different economic levels. The area surveyed is divided roughly into two large parts according to the nature of staple cereals consumed by the families—rice and jawar. It can be seen from table I that the diet of jawar eaters is better in quality than that of rice eaters, but the difference in quantity is negligible.

Incidence of deficiency diseases

The incidence of deficiency diseases among school children was investigated in each of the areas where dietary surveys have been made.

* Paper condensed by the editor.

TABLE I

Food intake in ounces among rice eaters and jawar eaters at different economic levels

Foodstuffs	GROUP I EARN- ING RS. 3 PER MENSEM		GROUP II EARN- ING RS. 3-6 PER MENSEM		GROUP III EARN- ING RS. 6-10 PER MENSEM		GROUP IV EARN- ING RS. 10-15 PER MENSEM	
	Rice eaters	Jawar eaters	Rice eaters	Jawar eaters	Rice eaters	Jawar eaters	Rice eaters	Jawar eaters
Total cereals	22.9	22.9	24.5	27.4	23.4	26.8	26.7	22.8
Milled rice	0.1	0.2	0.3	0.8	1.5	2.5
High polished rice (<i>Oryza sativa</i>) ..	14.2	..	16.3	0.1	16.1	0.1	17.7	0.6
Jawar (<i>Sorghum vulgare</i>)	2.1	22.1	3.5	24.7	2.4	22.7	4.1	15.2
Maize (<i>Zeamays</i>)	2.7	..	1.4	..	0.7	..	0.6	..
Bajra (<i>Pennisetum typhoideum</i>) ..	1.3	0.6	0.6	1.7	1.0	1.3	..	0.5
Italian millet (<i>Setaria italica</i>) ..	1.9	0.1	2.1	0.2	2.7	0.6	2.0	..
Ragi (<i>Eleusine coracana</i>)	0.8	..	0.5	..	0.2
Wheat (<i>Triticum vulgare</i>)	0.1	..	0.5	..	1.3	0.8	4.0
Pulses	0.7	1.0	1.3	1.4	1.7	2.3	2.4	4.0
Leafy vegetables	0.1	0.1	0.2	0.2	0.2	0.2	0.4	0.6
Non-leafy vegetables	0.2	0.1	0.4	0.3	0.6	0.7	1.4	1.5
Fats and oils	0.1	0.1	0.2	0.2	0.2	0.6	0.7	1.0
Milk	0.1	0.3	0.5	1.0	1.0	2.3	2.8	5.6
Curds	0.1	..	0.2	0.6	0.5	0.5	1.6	1.9
Butter milk	0.3	0.4	1.0	2.0	2.6	1.0	6.0	1.3
Meat, fish and eggs	0.3	0.3	0.2	0.3	0.2	0.3	0.3	..
Fruits	0.3	..	0.5
Sugar	0.6	0.3	0.2	1.6
Condiments	1.1	0.5	1.3	0.4	1.7	1.0	0.2	0.7

TABLE II

Incidence of Bitot's spots, phrynoderma and angular stomatitis amongst children in rice and jawar eating communities

Group	NUMBER OF CHILDREN EXAMINED		PERCENTAGE SHOWING BITOT'S SPOTS		PERCENTAGE SHOWING PHRYNODERMA		PERCENTAGE SHOWING ANGULAR STOMATITIS		PERCENTAGE SHOWING GLOSSITIS	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Rice eaters	9,722	771	4.3	1.9	Only 3 cases		3.9	1.0	0.7	0.4
Jawar eaters	4,947	1,775	2.9	1.6			2.7	0.9	0.06	0.1

Children have been examined in preference to adults because they are more delicate agents for the detection of deficiency diseases.

Table II shows the percentage of deficiency diseases amongst them.

Bitot's spots.—In the investigation, all degrees of dryness of conjunctivæ were seen, but we have included only cases showing Bitot's spots because they can be seen even when they are just the size of a pin-head and it is a convenient and definite sign in routine examination for recording vitamin A deficiency.

Phrynoderma or follicular keratosis.—Out of 18,000 children examined, we came across only 3 typical cases, whereas Bitot's spots were present in 10 per cent of children examined. Both these diseases are supposed to be due to vitamin A deficiency, but such great disparity in the incidence of the two diseases confirms

the view that phrynoderma is not caused by a simple vitamin A deficiency.

Angular stomatitis.—It is decidedly more amongst rice eaters, though they consume home-pounded rice, and this can be attributed to faulty way of cooking rice; washing it repeatedly, and throwing away the water used, depletes it of B vitamins.

Jawar is rich in riboflavin and one should not expect to find glossitis or angular stomatitis amongst jawar eaters. These symptoms were present only amongst those who ate it in the form of 'ghatka.' In this preparation jawar is first steeped in water, partly dried and then pounded till the outer layer is separated. This is sieved off and the remaining portion is washed and cooked, most of B vitamins thus being presumably lost. It was interesting to

find that those who took 'chappaties' made out of jawar flour did not suffer from this deficiency.

Scurvy and rickets.—No typical cases of scurvy or rickets were detected amongst the children of both the areas.

The lower incidence of deficiency diseases among jawar eaters, when compared with that observed in rice eaters, is the result of the better

figures were correct to within six months, any error in one direction cancelling out that in the opposite direction. Height measurements were taken standing, to the nearest tenth of an inch. Weight was recorded to the nearest quarter pound by an Avery's lever balance. The results are given in tables III and IV.

From table III it will be observed that the Hindu boys tend to be shorter and lighter than

TABLE III

Height and weight of Mohammedan and Hindu boys of jawar eating areas (Marathwada)

Age in years	HEIGHT IN INCHES				WEIGHT IN POUNDS	
	Mohammedans		Hindus		Mohammedans	Hindus
	Number	Examined	Number	Examined		
5	63	41	75	41	32½	34
6	150	43	181	43	36½	36½
7	255	46	285	44½	41	38
8	320	46½	279	46	44½	42½
9	362	49	315	48	48	46
10	436	50½	383	48½	50	49
11	363	51	288	51½	54	54½
12	463	53½	287	55	60½	59½
13	375	56	174	54½	67½	65
14	718	60½	448	60	82½	83
and above.						

TABLE IV

Height and weight of Mohammedan and Hindu boys of rice eating areas (Telengana)

Age in years	HEIGHT IN INCHES				WEIGHT IN POUNDS	
	Mohammedans		Hindus		Mohammedans	Hindus
	Number	Examined	Number	Examined		
5	97	39	100	39	31½	31½
6	231	40½	200	40	33	33
7	358	43	353	42	36	36½
8	472	45	439	45	39½	39½
9	379	46½	371	46½	43	42
10	550	49	449	48½	47	46½
11	466	50½	374	50½	49½	50½
12	626	52½	606	52	55	54
13	463	54½	412	54½	60½	62
14	779	59	654	59	75½	75½
and above.						

quality of their diet. Jawar eaters include milk and its products to some extent in their diet.

Physical development.—The age, sex, height, and weight of the children were recorded. Age last birthday as entered in the school register was recorded and it was assumed that these

the Muslim boys of the same age in jawar eating areas. Table IV shows that there is almost no difference in height and weight among Mohammedan and Hindu boys in rice eating areas. It is also seen that jawar eaters tend to be taller and heavier than rice eaters whether they are Mohammedans or Hindus.

Current Topics

Evaluation of Penicillin in Gonorrhœa Treatment and Control

By R. A. KOCH, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 13th October, 1945, p. 491)

1. Of 485 gonorrhœa patients treated with an initial course of 200,000 units of penicillin, 68 (14 per cent) were not cured.
2. Hospitalization of gonorrhœa patients does not appear to affect the failure rate. This would indicate that failures occurring in out-patients are probably not reinfections.
3. Minimum criteria of cure, including multiple cultures in penicillin-treated gonorrhœa patients, are indispensable to the public health control of the disease.
4. We cannot definitely report a case of complete penicillin resistance; however, 1 in 7 failed on the first course of treatment, many of the retreated ones required more than one repeat course, and in some of them sulphonamides and pyrotherapy were administered simultaneously.
5. We have been unable to confirm the necessity for the usually accepted practice of differentiating gonococci from other members of the *Neisseria* family by sugar fermentation tests; 350 laboratory observations, although not conclusive evidence, constitute a not inconsiderable group on which to base an opinion.
6. In the control of gonorrhœa the medical profession must be aware of the limitations of penicillin therapy, the possibility of producing a carrier state and the social factors related to the spread of the disease.

Nutritional Macrocytic Anæmia

(From the *British Medical Journal*, ii, 13th October, 1945, p. 501)

THE sternal puncture needle, by enabling us to study the bone marrow almost as easily as we can the blood, has cleared up some of the obscurity about pernicious anæmia and its congeners. We know now that the pathognomonic feature of this large group of deficiency diseases of the blood-forming organs is the proliferation of megaloblasts in the bone marrow and the restoration of the normal type of erythropoiesis by liver. This may take place in circumstances in which the peripheral blood is not frankly megalocytic, as in some cases of pernicious anæmia of pregnancy and tropical macrocytic anæmia. On the other hand, the blood picture in aplastic and hæmolytic anæmias may sometimes be megalocytic, but the bone marrow is not megaloblastic and treatment by the pernicious anæmia (P.A.) factor is ineffective. In accordance with Castle's hypothesis of extrinsic and intrinsic factors the megalocytic deficiency anæmias can be further subdivided into those which are due to a defect in the diet, the nutritional macrocytic anæmias, and those which are due to a disturbance in the digestion, of which Addisonian pernicious anæmia and sprue are the chief examples. This distinction must not be pressed too far, for dietary deficiencies have a way of impairing digestion, as has been only too sadly verified in recent experiences of starvation in Europe. The laboratory data in nutritional macrocytic anæmia differ in three ways from those commonly found in pernicious anæmia: (1) hydrochloric acid is usually present in the gastric juice; (2) the serum bilirubin is within normal limits; and (3) the serum iron is usually not elevated.

Nutritional macrocytic anæmia is so prevalent that it might have been expected that the enormous number of cases would have enabled us to work out the chemistry of the extrinsic factor and the P.A. principle. Unfortunately this has not yet happened. It is difficult to carry out controlled therapeutic trials in tropical and subtropical countries owing to the poverty of hospital and laboratory resources and the temperament of the patients. Moreover, like most dietary defects, nutritional macrocytic anæmia is often complicated by multiple deficiencies, and by infections and parasitic infestations. A deficiency of iron so frequently occurs at the same time that the useful name 'dimorphic anæmia' has been introduced. Hæmolysis may be provoked by concomitant malaria, and pregnancy is a common cause for the final breakdown. Nutritional macrocytic anæmia is also more often resistant to treatment than Addisonian pernicious anæmia, particularly to treatment by highly purified extracts of liver. This has led to the suggestion that whole liver and proteolysed extracts of liver contain active principles which are lost during purification. It is possible, however, that the difference is merely one of dosage; with purified intramuscular extracts it is unusual to give more than 0.2 g. of liver solids a day, while with proteolysed extract of liver the dosage is 50 g. a day. Moreover, resistance is sometimes due to recognizable inhibitory influences such as pregnancy or infection, and it is not in itself a strong argument for a chemical difference in the nature of the hæmatinic principles which are lacking in pernicious anæmia and nutritional macrocytic anæmia. Nevertheless, all these complications make research on nutritional macrocytic anæmia a difficult and tedious business.

Much confusion has existed about the pathogenesis of the macrocytic anæmia of pellagra and other forms of vitamin-B deficiency. The incidence of this anæmia varies widely in different parts of the world and in the different types of avitaminosis B. In Egypt, Salah found no macrocytic anæmia among 118 pellagrins. In endemic pellagrous areas of the United States, Huck and Turner found anæmia uncommon, and, when present, usually hypochromic and microcytic in character. Among the so-called alcoholic pellagrins, Spies and Chinn found macrocytic anæmia to be relatively common. The anæmia has been variously ascribed to lack of specific B factor, deficiency of Castle's extrinsic factor, and loss of the intrinsic factor. Since the B complex and the extrinsic factor are often closely associated in nature and since pellagrous diets are frequently deficient in both, it has hitherto been difficult to determine which, if either, plays the decisive part in the production of the anæmia. The frequency of absolute achlorhydria in pellagra has lent support to the view that the anæmia results from absence of the intrinsic factor. Nevertheless, little information has been available about the intrinsic factor of the gastric juice in this disease; it has been demonstrated in a few instances, but only in patients in whom there has been no significant anæmia. Furthermore, the incidence of achlorhydria appears to vary; Sodeman found it in 55 out of 77 pellagrins, whereas Moore, Vilter, Minnich, and Spies demonstrated free HCl in the gastric juice at one or another time in as many as 21 out of 25 pellagrous patients.

The question of the pathogenesis of this anæmia has now been decisively answered by Moore and his co-workers. They have studied 25 patients with pellagra in whom glossitis, dermatitis and peripheral neuritis were associated with a severe macrocytic anæmia. The diets of these patients had for many years been grossly deficient in all the members of the B complex and in animal protein. The anæmia was cytologically indistinguishable from Addisonian anæmia, but in 21 of the 25 patients free hydrochloric acid was found in the gastric juice. The American workers were able to demonstrate the presence of intrinsic factor in the gastric juice of two of their cases by the production of a reticulocyte response when patients with Addisonian anæmia were treated with a mixture of pellagrous gastric juice and extract of raw beef



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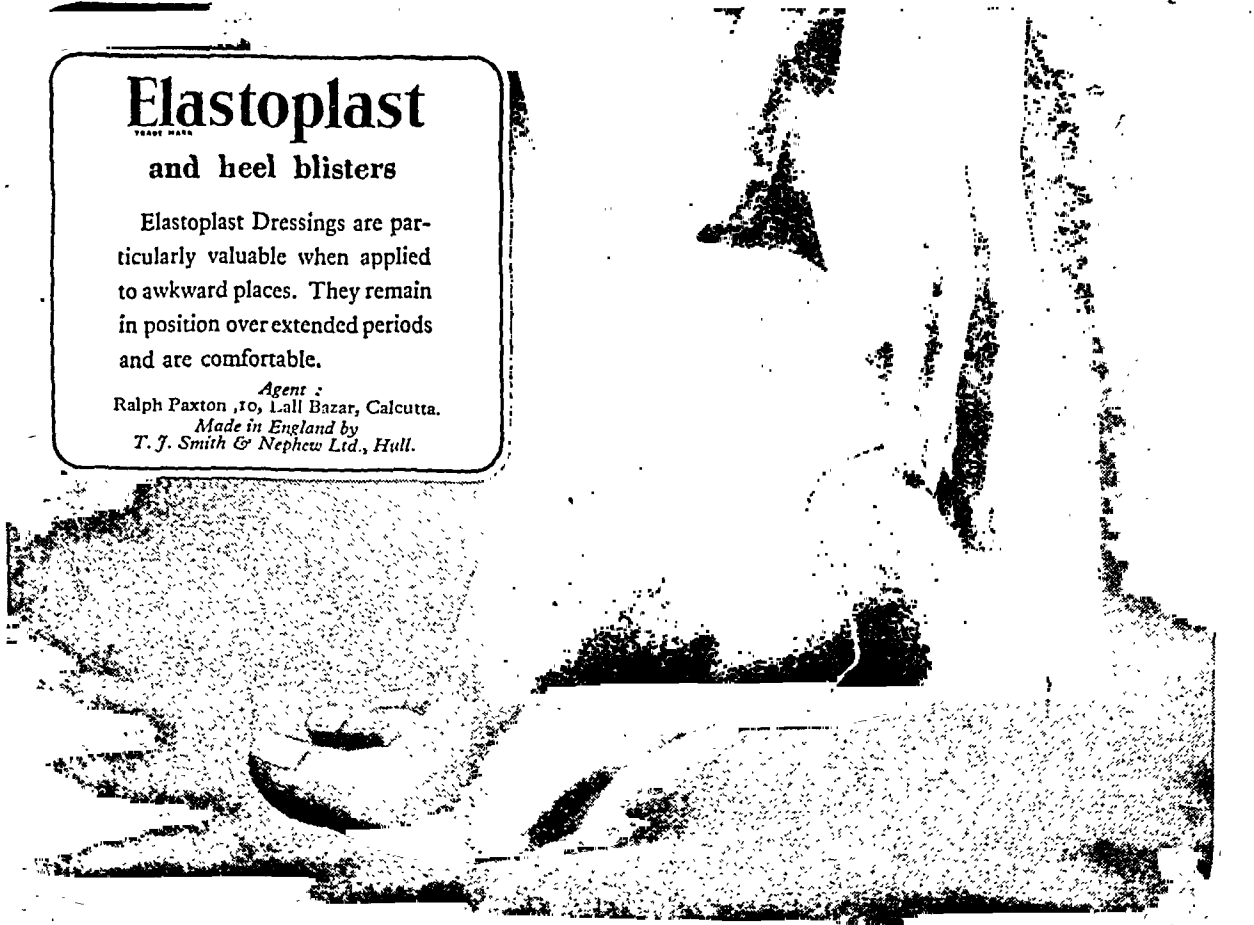
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muscle. Having shown in this way that the anaemia was not due to an intrinsic defect, they then proceeded to study the reticulocyte response in the pellagrins while they were kept on a standard diet deficient in both the B complex and Castle's extrinsic factor, in order to determine the specific nutritional deficiency responsible for the anaemia. After a control period on the diet, massive oral and parenteral therapy with all the known B vitamins was tried, and though the clinical manifestations of avitaminosis were relieved there was no change in the reticulocyte count. Nicotinic acid, thiamine, riboflavin, calcium pantothenate, pyridoxine, inositol, para-aminobenzoic acid, and choline had no therapeutic value in correcting the anaemia even though they were given in combination both orally and parenterally. Administration of highly purified liver extracts, however, caused prompt haematological and clinical improvement. When extract of raw beef muscle was ingested daily a suboptimal reticulocyte response occurred which was followed by a rise in the red cell count and clinical remission. In one of these patients there was a further small rise in the reticulocytes when a mixture of normal human gastric juice and beef extract was ingested, and again an increase in reticulocytes followed by acceleration of the rise in red cell count when purified liver extract was given parenterally. All the patients, in whom the reticulocyte response was suboptimal when beef extract was ingested, exhibited a second reticulocyte response after intramuscular injection of purified liver extract.

Moore and his colleagues conclude that none of the B vitamins they used can act as the extrinsic factor, and that the macrocytic anaemia of pellagra depends on a prolonged deficiency of Castle's extrinsic factor in the diet. This is associated in many instances with poor absorption from the gastro-intestinal tract and in some cases with inadequate production of intrinsic factor by the gastric mucosa. Most of the patients were observed for two or three years, and, as would be expected, the few who corrected their faulty dietary habits remained well without further liver therapy. These findings provide an explanation of the variable incidence of macrocytic anaemia in pellagra. Though the sources of the B complex and the extrinsic factor are frequently identical, deficient dietaries may be lacking in one or other as well as in both. A high incidence of macrocytic anaemia unaccompanied by avitaminosis has recently been reported in this journal among Indian troops on an exclusively vegetarian diet, whereas it is probable that the diets of pellagrins in Egypt and the endemic areas of the United States, where the incidence of macrocytic anaemia is low, contain adequate amounts of the extrinsic factor though deficient in the B complex.

Finally, we must emphasize that this excellent American study is a challenge to British haematology. The British Empire is the world's largest reservoir of nutritional macrocytic anaemia, and it is painful that English haematologists should be expending their skill on the minutiae of their craft at home when such important work awaits them in the field. A cheap remedy for nutritional macrocytic anaemia would greatly enhance the vigour of tropical and subtropical populations. To discover it there are some obvious immediate steps. The first is the creation of a research centre or centres in a situation where large numbers of patients with nutritional macrocytic anaemia can be attracted and treated. The second is the fractionation of beef muscle by the same kind of technique as the Harvard group has developed for plasma and the study of the separate fractions to locate and isolate the extrinsic factor. The third is the purification and characterization of the liver principle. These problems have hung in the wind for the last ten years, largely as a result of the war and the impossibility of sending research teams overseas, but the war itself has shown how important the problem of nutritional macrocytic anaemia is, and how urgent, therefore, it is to create an organization to deal with it.

Intravenous Nutrition for Eight Weeks : Partial Enterectomy, Recovery

By A. BRUNSCHWIG
R. BIGELOW
and
S. NICHOLS

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 6th October, 1945, p. 441)

A PATIENT with a large upper jejunal fistula received intravenous casein digest, dextrose and saline solution intravenously for a period of eight weeks. No food was ingested by mouth. After forty-six days laparotomy for partial enterectomy and entero-enterostomy were performed, closing the fistula. Recovery was uneventful, intravenous nutrition being continued for nine days after operation. The experience in this case suggests that intravenous nutrition permitting the withholding of food by mouth might prove beneficial in the management of large fistulas high in the small bowel, since discharges from the fistulas would be appreciably reduced and thus permit a degree of healing which might then be completed by surgical closure.

Urinary Excretion of Coproporphyrin in Non-Alcoholic Pellagra

By C. RIMINGTON
and
Z. A. LEITNER

(Abstracted from the *Lancet*, ii, 20th October, 1945, p. 494)

URINARY coproporphyrin excretion has been found, except in two cases explicable on other grounds, to lie within normal limits in a series of 15 non-alcoholic pellagra patients whose prompt and satisfactory response to nicotinic-acid medication substantiated the diagnosis of their condition.

In a series of 7 patients with Korsakoff's syndrome, in 6 instances referable to alcoholism, only 2 showed abnormally high urinary porphyrin excretion.

A case of beri-beri (alcoholic) had a marked porphyrinuria, which remained unchanged despite appropriate medication and much improvement in general condition.

These studies further emphasize that porphyrinuria is not an essential feature of pellagra, and that determination of urinary porphyrin does not in any way aid in the diagnosis of the condition. Alcoholism *per se* appears to be insufficient necessarily to produce porphyrinuria.

The factors or combination of factors which may lead to porphyrinuria in persons with pellagra, simultaneously exposing their livers to assault by quantities of alcohol, have been considered in the light of recent findings relating extent of hepatic injury to level of intake of an essential factor, such as protein or methionine, in the presence of a toxic agent.

Infective Hepatitis Transmission by Faeces and Urine

By C. M. FINDLAY
and
R. R. WILLCOX

(Abstracted from the *Lancet*, ii, 10th November, 1945, p. 594)

OF 99 recipients of possibly infected material, faeces or urine, 24 are regarded as having given a positive response: 12 with definite icterus and the symptoms of infective hepatitis, 12 with subicterus but biochemical

changes in urine and blood and slight symptoms. Of the primary inoculations which were positive 12 had definite icterus, and 4 were subicteric; of the 8 positive second passages all were subicteric. If the persons receiving neoarsphenamine are discarded, there are 18 positives; but for the reasons given it is not considered that the injections of neoarsphenamine were alone responsible for these 6 positives.

The explanation for this comparatively low proportion of positives might be destruction of the causal agent by the gastric juice and pre-existing immunity.

One of the many disadvantages of working with human volunteers is that their past history is unknown. As pointed out by Pindlay, Martin and Mitchell, the immunity induced by one attack of infective hepatitis is probably considerable in view of the small number of true second attacks. Since subicteric cases undoubtedly occur during outbreaks of infective hepatitis, the chances of exposure to virus and thus the possibility of acquiring immunity must be by no means infrequent among the general population.

The experiments here recorded confirm those of Voegt, who claimed to have produced infection in man by oral administration of urine. The results with faeces agree with those of other workers who have produced icteric and subicteric infections.

It would seem probable that the virus of infective hepatitis has two possible portals of entry: through the nasopharynx as a droplet infection, and through the alimentary canal as the result of contamination of food by infected faeces or urine. Experimentally the disease can also be transmitted by subcutaneous injection.

Summary

Typical icteric and subicteric cases of infective hepatitis have developed after the oral ingestion of faeces or of urine from spontaneous cases of infective hepatitis.

Faeces filtered through a Seitz filter proved infective in one experiment.

Subicteric cases only have resulted from the oral ingestion of faeces or of urine from experimentally produced infections.

There is suggestive evidence that concurrent injections of neoarsphenamine increase the liability to positive results.

Sulphonamides in Bacillary Dysentery

By J. G. SCADDING

(Abstracted from the *Lancet*, ii, 3rd November, 1945, p. 549)

THE only definite conclusions that can be drawn from these and my previous observations is that the absorbable sulphonamides, even in small doses, were at least as effective as, and possibly more effective than, the poorly absorbable sulphonamides in the treatment of bacillary dysentery of the type at present seen in ME. On the question of the effectiveness of the sulphonamides in general, no statistically satisfactory evidence was obtained, though the clinical impression that severe and some chronic cases benefited, especially from moderate doses of sulphadiazine, was strong. The observations were relevant only to the therapy of the individual case; the important question of the effect of sulphonamides on the carrier state was not investigated.

Therapeutic Effect of Induced Jaundice in Rheumatoid Arthritis

By F. GARDNER, *et al.*

(Abstracted from the *British Medical Journal*, ii, 17th November, 1945, p. 677)

JAUNDICE was induced in 32 patients with rheumatoid arthritis, and temporary improvement in the latter condition was obtained in 25 cases.

The remissions were unequal in degree and of short duration. Ten patients became completely free from pain and swelling, and 15 showed some improvement. The average period during which optimal improvement was observed was 42 days, but a longer time elapsed before the joints reverted to their pre-icteric condition.

Complete freedom from pain and swelling was obtained more often in patients who had had rheumatoid arthritis for less than 5 years than in those who had it for more than 5 years.

There was no definite relationship between the intensity of the jaundice and the type of remission evoked.

In many cases a fall in the E.S.R. was noticed during the icteric phase. This was followed by a rise to a level above that recorded before jaundice was induced. These changes did not necessarily correspond to changes in the joint condition. A similar phenomenon has been observed when patients with active tuberculosis develop infective hepatitis.

The suggestion is put forward that improvement in the joint condition and the changes in the E.S.R. may be related to changes in the plasma proteins, but no evidence is available to support this view.

The induction of jaundice in rheumatoid arthritis is justifiable only as a research measure. Its aim is to identify the substance or mechanism responsible for the remission of the joint condition and ultimately to reproduce this mechanism by other less dangerous methods.

Therapeutic Effect of Induced Jaundice

By E. MUIR

(From the *British Medical Journal*, ii, 1st December, 1945, p. 782)

REFERRING to the article by Drs. Frances Gardner, Alice Stewart, and F. O. MacCallum (17th November, p. 677) on the therapeutic effect of induced jaundice in rheumatoid arthritis, some twelve years ago I noticed in a patient with leprosy, with lesions of the major tuberculoid type scattered all over the body, and who acquired severe jaundice, that all the lesions disappeared; also as the erythrocyte sedimentation rate was being tested every 7 or 14 days in the hospital where the patient was, I noticed that the E.S.R. fell rapidly. The effect was so striking that I considered the question at the time of inducing jaundice as a therapeutic measure in leprosy, but was not successful in doing so.

About 18 months ago I had another case in which a woman had leprosy lesions of a similar nature and who acquired an acute hepatic condition with severe jaundice. Within a few days all her lesions disappeared, and a few weeks later her hepatic conditions cleared up temporarily and she seemed to be in excellent health. The latter condition, however, returned and ended fatally but there was no return of the leprosy lesions.

I think these records are worth considering, especially as mention is made in this article of a similar improvement in tuberculosis, a disease which so closely resembles leprosy in every respect.

Cultivation of *Rickettsia Tsutsugamushi* in Lungs of Rodents: Preparation of a Scrub-Typhus Vaccine

By F. FULTON

and

L. JOYNER

(Abstracted from the *Lancet*, ii, 8th December, 1945, p. 729)

A METHOD is described of adapting *Rickettsia tsutsugamushi* to grow in the lungs of mice. Still better

yields were obtained by passing the mouse-lung-adapted strain into the lungs of cotton-rats. A vaccine prepared from cotton-rat lung suspension protected mice subsequently infected with living *R. tsutsugamushi*. The best protection was obtained when the mice were vaccinated intraperitoneally and challenged by the same route, but some protection could also be demonstrated when the mice were vaccinated subcutaneously and challenged by the intraperitoneal route. Arguments are presented to show that, without a field trial, it is impossible to decide whether this vaccine will be of any value in man.

Optimum Dose of Sulphadiazine in Treatment of Pneumococcic Pneumonia

By M. F. COLLEN
and
E. PHILLIPS

(From the *Archives of Internal Medicine*, Vol. LXXVI, July 1945, p. 22, as abstracted in the *International Medical Digest*, Vol. XLVII, November 1945, p. 274)

THE treatment of patients with pneumococcic pneumonia with double doses of sulphadiazine resulted in (1) a decrease in the gross mortality from 10.7 to 6.2 per cent (corrected for patients dying within six hours after their hospitalization, the mortality rate decreased from 10.2 to 5.5 per cent), (2) a decrease in the incidence of sterile pleural effusions from 5.2 to 2.7 per cent, and (3) a decrease in the average number of days in the hospital required for recovery (66 per cent required less than seven days, as compared to 45 per cent).

There was no greater incidence of drug toxicity in patients treated with double doses of sulphadiazine than in those treated with usual doses.

Chemoprophylaxis in Wounds

(From the *International Medical Digest*, Vol. XLVII, November 1945, p. 310)

WHAT was regarded as an indispensable part of the equipment of every combat soldier in the recent war, was a packet of sulphanilamide to shake into their wounds and even tablets to swallow. Now many will be surprised, and perhaps disappointed, to learn that a recent investigation by Meleney reveals that this prophylactic measure was not as effective as originally believed. His study deals with a total of 2,191 cases, of which 926 were wounds of soft parts, 674 compound fractures and 591 burns. They were treated in nine different centres, where records were kept in a uniform manner subsequent to analysis. No uniform system of sulphonamide treatment was adopted, the cases being divided into those which received it in any form, whether local or general, and those which did not. The number of control cases was about equal to the treated burns, but only one-third in the other two groups. Some difficulty was found in providing adequate controls, particularly at centres where sulphonamide prophylaxis had been a routine procedure.

Analysis and tabulation into 46 groups indicates that the treated cases were rather more severe than the controls. The frequency of infection depended largely on such factors as the extent of tissue damage and of subsequent contamination. No evidence whatever was discovered to indicate that sulphonamide prophylaxis reduced the frequency of infection. The controls on the whole fared somewhat better. Apparently what sulphonamides locally will not do, according to these results, is to reduce liability to either trivial or serious infections. So this routine practice seems to be useless and the taking of tablets in anticipation of trouble may be harmful.

The results of these studies will be regretted just as Meleney regretted his discovery. Any way, the U.S.

Army has discontinued the use of sulphanilamide chemoprophylaxis according to recent information.

Effect of Large Doses of Alkali on Kidney Function

(Abstracted from the *Lancet*, ii, 1st December, 1945, p. 701)

THE investigations described here were undertaken to study in normal subjects the effects of the intensive alkali treatment that is still being recommended in blackwater fever, incompatible blood transfusion, and crush syndrome. For instance, the Medical Research Council recommended that in the treatment of wound shock 'all cases should be given sodium bicarbonate 7 g. (2 oz.)' (*sic*) 'hourly by mouth until the urine turns red litmus blue, but not for longer than 24 hours'.

Intensive alkali therapy of this kind is accompanied by dangers, and its efficacy is open to question. The results of the experiments described in this paper show that alkali, administered for 24 hours to normal subjects at less than half the rate recommended above, produces sodium and water retention and disturbances of renal function, which become well marked if the alkali is continued for 72 hours.

SUMMARY

Three subjects were given an extensive course of alkali consisting of sodium bicarbonate gr. 60 and sodium citrate gr. 60 2-hourly. One subject received this course for 1 day; two subjects for 3 days.

All the subjects on alkali had disturbances of renal function. In one, on the course for 3 days, this was well marked and led to a three-fold increase in blood-urea.

All the subjects on alkali developed fairly intense alkalosis, not entirely compensated, together with sodium and water retention. There was dilution of the blood by about 10 per cent.

Both the subjects on alkali for 3 days complained of symptoms.

A fourth subject was given an equivalent amount of sodium as sodium chloride for 24 hours. He showed a slight degree of sodium and water retention and no alteration of renal function.

The amount of alkali given in these experiments had measurable physiological effects, including disturbances of renal function. We consider, therefore, that large doses of alkali should not be administered in conditions where renal failure may supervene.

Sulphadiazine Resistant Strains of Beta Hæmolytic Streptococci

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, December 1945, p. 921)

AFTER approximately three months of successful sulphadiazine prophylaxis of respiratory infections at a large naval training centre, the effectiveness of this measure became progressively less and eventually a major epidemic of streptococcal disease occurred.

An increase in dosage as high as 2 gm. daily did not prevent streptococcal diseases, and it was the impression of medical officers at the centre that the drug had lost its value therapeutically in these infections.

The loss of prophylactic value of sulphadiazine was originally associated with an absolute and relative increase in the frequency of group A, type 19 infections to the practical exclusion of all other types. Later, group A, type 17 became relatively frequent. These two types were shown by laboratory methods to be sulphonamide resistant *in vitro*.

Other types of streptococci with a few exceptions of type 3 were not sulphonamide resistant.

The proportion of sulphadiazine resistant strains was greater in those recruit camps getting sulphadiazine prophylaxis than in those not getting sulphadiazine.

There was some suggestive evidence but no definite proof that, in the presence of sulphadiazine resistant strains, sulphadiazine prophylaxis tended to increase streptococcal infection, particularly scarlet fever.

Bacitracin : A New Antibiotic

(From the *Journal of the American Medical Association*, Vol. LXXIX, 1st December, 1945, p. 953)

In a study of the bacterial flora of contaminated wounds, Johnson and his associates of the departments of surgery and biochemistry, Columbia University College of Physicians and Surgeons, found that pathogenic micro-organisms appeared at times on blood agar plates following direct plating of the injured tissues; these were not demonstrable in broth cultures made at the same time from the same material. This occurred most frequently when the broth cultures contained non-pathogenic contaminants of the *Bacillus subtilis* group. Many of these contaminants had an inhibiting action on subsequent platings with gram-positive cocci, one strain being of particularly high antibiotic titre. The active principle of a cell-free filtrate from this strain has been named 'bacitracin' by the Columbia University investigators.

'Bacitracin' is formed by surface growth of this strain on a variety of liquid mediums but not in submerged growths, the maximum titre being reached after three to five days' incubation at 37°C. This antibiotic is insoluble in ether, chloroform, acetone or ethyl acetate but can be extracted from broth cultures with normal butanol. Evaporation of the butanol extract by steam distillation *in vacuo* results in a greyish white powder.

'Bacitracin' thus prepared is a neutral substance not precipitable by manipulating the pH. In this it differs from other earlier antibiotics. The substance is water soluble and coagulable. It is non-haemolytic for human or sheep erythrocytes and resists digestion with pepsin or trypsin. The substance is non-toxic on intraperitoneal or intravenous injection into laboratory animals or on subcutaneous injection into human volunteers. It is non-irritating when applied to the human conjunctiva.

A tentative standard 'unit' of bacitracin was adopted by the Columbia University surgeons, an amount which diluted 1,024 times and added to 2 c.c. of beef infusion broth will completely inhibit the growth of a stock culture of haemolytic streptococci. This is apparently about 500 times the Oxford unit used in standardization of penicillin. Adopting this unit, the material obtained by harvesting from a synthetic culture medium at times assays as high as 10 Columbia units per cubic centimetre (the equivalent of 5,000 Oxford units). This abundant yield would be of trade interest if the new product should be produced commercially.

The new antibiotic is active against a wide range of pathogenic micro-organisms. From 0.001 to 0.002 Columbia unit gives complete bacteriostasis with standard suspensions of pneumococci, haemolytic streptococci and *Clostridium welchii*. Slightly larger doses are required for complete inhibition of *Clostridium histolyticum*, gonococci and meningococci. *Escherichia coli* and *Proteus vulgaris* are not inhibited.

In vivo protection tests have been made on mice injected intraperitoneally with 10,000 minimum lethal doses of haemolytic streptococci. If this inoculation is followed at three-hour intervals for thirty-six hours by subcutaneous injections of 1 unit of bacitracin, approximately 90 per cent of the injected mice survive. The control mortality is 100 per cent. Guinea-pigs similarly injected with multi-lethal doses of *C. welchii* or *C. septicum* are 100 per cent protected by repeated subcutaneous injections of bacitracin.

Thus far bacitracin has been used locally to treat a number of human infections due to haemolytic strepto-

cocci and staphylococci. The results are equal to the response in similar cases to local penicillin therapy. Attempts are now being made to produce bacitracin by large scale commercial methods. If successful, the new antibiotic should be much cheaper than penicillin.

Indian Journal of Medical Research

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3. Bose, S. M., and Banerjee, B. N. Studies on the destruction of vitamin A in shark-liver oil. Part V. Effect of some anti-oxidants on the stabilization of vitamin A.
4. Bashir Ahmad, Ram Chand, and Mansoor-ul-Hassan. Vitamin A content of the liver oils of common fresh-water fishes of the Punjab.
5. Mason, Eleanor D., Theophilus, Florence, and Frimodt-Møller, J. The influence of butter fat in the absence or presence of casein on growth in young rats on a rice diet.
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7. Shourie, K. L. An outbreak of lathyrism in Central India.
8. Patel, T. B. Nutrition and dietary surveys in Bijapur District (Bombay Presidency), at the end of the famine year of 1943.
9. Pai, M. L. Blood urea clearance in Indians.
10. Bose, B. C., and Mukerji, B. Observations on the physiologically active fraction of Indian hemp, *Cannabis sativa* Linn.
11. Hynes, M., Ishaq, M., and Morris, T. L. Anaemia in Indian army recruits.
12. Veeraraghavan, N. Cultivation of a protozoal parasite of the central nervous system *in vitro* and its relationship to rabies.
13. Veeraraghavan, N. A rapid method for the diagnosis of rabies in animals.
14. Khanolkar, V. R. The susceptibility of Indians to Cancer.

The authors' summaries of the articles are given below :

1. THE INCIDENCE, TYPE AND BACTERIOLOGY OF SALMONELLA INFECTION IN THE ARMY IN INDIA

A survey of Salmonella types responsible for disease in the army in India from 1941 to the beginning of 1945 has been made. Attention has been drawn to the marked increase in the number of *Bact. paratyphosum C* and *Bact. enteritidis* infections reported in recent years. By far the greater proportion of *Bact. enteritidis* strains have been isolated by blood culture or from anatomical sources which imply for the organism an invasive rôle in man. Possible reasons for the apparent increase in *Bact. paratyphosum C* and *Bact. enteritidis* infection are discussed. The clinical types of invasive *Bact. enteritidis* disease are described. An account is given of interesting or instructive findings in connection with the bacteriology of the Salmonella group.

2. STUDIES IN CALCIUM AND PHOSPHORUS METABOLISM. PART VII. THE IONIC PRODUCTS OF CALCIUM PHOSPHATES IN EXPERIMENTALLY INDUCED VITAMIN D DEFICIENCY

Vitamin D deficiency has been induced in dogs on two types of diets, one a diet deficient only in respect

of vitamin D and the second a diet deficient not only in vitamin D but in which the phosphorus content was very low. The serum calcium, serum inorganic and acid-soluble phosphorus, serum protein, and plasma pH were determined at fortnightly intervals throughout an experimental period lasting 16 to 31 weeks. The findings on these two diets are summarized separately.

(1) *On diet I.*—Serum calcium decreased as vitamin D deficiency increased; serum inorganic phosphorus as compared with the controls was only slightly reduced. On administration of vitamin D, the serum calcium rose earlier than the inorganic phosphorus. No significant change in the total acid-soluble phosphorus of the serum was observed. The protein content of serum slowly increased with age in both the control and the rachitic groups; vitamin D administration had no influence on the total serum protein of the rachitic dogs. The values for pK s.p. for CaHPO_4 and $\text{Ca}_3(\text{PO}_4)_2$ increased as the deficiency of vitamin D progressed, and decreased after the administration of vitamin D.

(2) *On low phosphorus diet.*—The young puppies used for this experiment showed a mild degree of rickets even at the beginning of the experiment. They were started on the same diet as in (1) but were later changed over to a low phosphorus diet. After this change hypercalcaemia set in in both the control and the rachitic groups. It set in earlier, however, in the control dogs, declining somewhat later on. The serum inorganic phosphorus was lower in the rachitic group and rose slowly after administration of vitamin D. The concentration of serum protein was unaffected by (a) the change in diet, (b) the onset of severe rickets, or (c) the administration of vitamin D. The plasma pH in both groups also remained unchanged throughout the experiment. At the beginning of the experiment the values for pK s.p. CaHPO_4 indicated undersaturation in all the four dogs. In control dogs receiving 500 I.U. vitamin D per day per dog they approached the saturation point whereas those of rachitic dogs moved slowly towards saturation even after the administration of 4,000 I.U. vitamin D per day per dog.

The observation made in clinical rickets that the ionic products of calcium phosphates are influenced by state of vitamin D nutrition has been confirmed.

3. STUDIES ON THE DESTRUCTION OF VITAMIN A IN SHARK-LIVER OIL. PART V. EFFECT OF SOME ANTI-OXIDANTS ON THE STABILIZATION OF VITAMIN A

While carrying out the storage tests, it was observed that there was no appreciable change of odour and taste during the induction periods of the oil samples; soon after, the oils developed a characteristic taste and sharp odour indicating that the onset of rancidity usually coincides with or follows shortly after the end of the induction period, and also the destruction of vitamin A generally proceeds as the oil develops rancidity.

Accelerated oxidation tests can give clear comparative estimates of the stability of the oils under actual storage conditions (Orson Bird, 1942). Recently, Lea (1944) has shown that the rapid 'sorting' tests at 100°C. and the storage tests at 37°C. agree well on the whole, in placing the various anti-oxidants in order of their efficiencies. In our experiments also, there is fairly good agreement between the relative potencies of the inhibitors, as observed at the two temperatures 75°C. and 40°C.

Most of the acid-type inhibitors and the amino-acids practically fail to protect the oil, with the exception of ortho-phosphoric acid. Among the phenolic inhibitors, hydroquinone protects vitamin A for a considerable period. The esters of gallic acid have proved more effective, the order of efficiency of the gallates and gallic acid being iso-butyl gallate, ethyl gallate, iso-amyl gallate, propyl gallate, methyl gallate, and gallic acid.

The synergetic effect of the gallates and the acid-type inhibitors is obvious. The maximum inhibiting action is obtained with a mixture of iso-butyl gallate and ortho-phosphoric acid; but the oil loses its original

colour and becomes darker and a black deposit is formed at the bottom of the specimen tubes. This is a drawback in actual practice. By using the salt, sodium dihydrogen phosphate, the difficulty of discoloration does not arise, but the inhibiting action is much retarded.

The combination of iso-butyl gallate and citric or tartaric acid is next best in merit. This combination does not discolour the oil, nor impart any foreign flavour to it. The occurrence of citric and tartaric acids in our everyday foodstuffs is well known and hence no objection can be raised to their use in shark-liver oil. The gallates also are usually considered non-toxic. The non-toxicity of propyl gallate has been indicated by Boehm and Williams, Gunn and Macdonald have reported the non-toxicity of ethyl gallate. There is, however, no such record of the non-toxicity of iso-butyl gallate in the literature; but for the very low concentration used, it is expected that the gallate will not be harmful. As suggested by Boehm and Williams under actual storage conditions, far lower concentrations of anti-oxidants may provide sufficient protection to the oil.

There is a slight drawback in using the gallates and the organic acids in shark-liver oil, viz, they are not perfectly soluble in the oil at room temperature. It has been observed, however, that after incorporating the mixtures of iso-butyl gallate (0.02 per cent) and citric or tartaric acid (0.01 per cent) in the oil, if it is kept for about 3 hours at 40°C., they completely dissolve in it and do not again settle out.

The preparation of the gallates is easy and inexpensive. The esterification of the homologues can be achieved by dissolving gallic acid in the corresponding hot alcohol, saturating the solution with dry hydrochloric acid gas and then refluxing for some time.

Hence the combination of iso-butyl gallate and citric or tartaric acid appears to be the best anti-oxidant, so far examined, for shark-liver oil. There is, however, scope for further investigation for selecting better preservatives.

4. VITAMIN A CONTENT OF THE LIVER OILS OF COMMON FRESH-WATER FISHES OF THE PUNJAB

The liver oils of some common species of fish found in the streams and rivers of the Punjab have been examined for their vitamin A content both by the colorimetric and spectrographic method of assay. They have been found to be rich sources of vitamin A. Values as high as 20,000 I.U. and 26,000 I.U. per g. have been recorded. The livers which are now allowed to go waste could yield appreciable quantities of medicinal fish-liver oils.

5. THE INFLUENCE OF BUTTER FAT IN THE ABSENCE OR PRESENCE OF CASEIN ON GROWTH IN YOUNG RATS ON A RICE DIET

The purpose of the present investigation was to examine the supplementary effects of casein, calcium lactate and butter, singly or combined, on the growth of young rats fed on a basal rice diet similar to that common among the poor in South India. Casein as well as calcium lactate was found to have a highly significant effect in promoting growth. Butter affected both growth rate and general condition adversely. Casein when added to butter counteracted the negative effect of butter and converted it into a positive effect. This interaction was highly significant. There was no significant interaction between calcium lactate and butter or between calcium lactate and casein. It is concluded that the poor rice diet is deficient in a factor or factors essential for the utilization of dietary fat and that this factor is supplied in technical casein.

6. INVESTIGATIONS ON THE NUTRITIVE VALUE OF TAPIOCA (*Manihot utilissima*)

The nitrogen complex of tapioca (*Manihot utilissima*) was investigated. A major portion of the nitrogen exists in the form of simple nitrogenous compounds. An attempt was made to isolate the proteins of the root in pure form. Both the protein and non-protein

fractions contain the amino-acids, tyrosine, tryptophane and cystine in fair amounts and have a high arginine content. *In vitro* digestibility experiments showed that the digestibility of tapioca proteins was not inferior to that of rice protein. The chief defect of tapioca as a source of protein appears to lie in its low total protein content rather than in the quality of the protein present. The digestibility of the carbohydrates of tapioca by two enzymes has been studied and found to be 48.3 per cent in raw state and 77.9 per cent after cooking. The starch is digested to a greater extent by taka diastase than by pancreatic amylase.

7. AN OUTBREAK OF LATHYRISM IN CENTRAL INDIA

An outbreak of lathyrism in Central India has been investigated. This was associated with the consumption of *Lathyrus sativus* in large quantities for a period of six months or more. Some 1,200 cases occurred in the district. Of these, 150 were seen, and full notes of 73 cases were taken. Villagers in the area in question and patients who contracted the disease realized that it was due to the consumption of this pulse. They also realized that it is not an infectious disease and understood its association with poverty. The chief sufferers from lathyrism were young adult males belonging to the poorest classes. September and October were the months of greatest prevalence. Clinically the disease manifests itself as a spastic paralysis of the lower limbs. The sphincters of the bladder and the rectum are not affected. No mental or sensory disturbances were observed. No *Vicia sativa* seeds were found in the stocks of lathyrus seeds consumed in the villages in which the outbreak occurred. The investigation points to the existence in *Lathyrus sativus* of a toxin affecting the pyramidal tracts. Preventive measures are discussed.

8. NUTRITION AND DIETARY SURVEYS IN BIJAPUR DISTRICT (BOMBAY PRESIDENCY), AT THE END OF THE FAMINE YEAR OF 1943

A dietary survey of 42 families in different income groups was carried out during the end of famine year 1943. The average calorie intake was sufficient in all income groups but some 33 per cent of families in the lower income groups consumed below 2,600 calories. Diets were deficient as regards animal protein, animal fat and calcium in all groups, vitamins A and C intake was also deficient in a number of families. The quality of diet showed improvement with the increase in income. Children belonging to different income groups, 5,131 in number, were examined for deficiency diseases and state of nutrition. The effects of famine conditions were reflected in a lowered state of nutrition of children, in an abnormally high prevalence of vitamin A deficiency, and to a lesser extent in the prevalence of vitamin C deficiency. There was also an increased death rate among infants and children between 1 and 10.

9. BLOOD UREA CLEARANCE IN INDIANS

A study of non-protein nitrogen content of serum and of blood urea clearance test in 32 patients has been presented. Most of these patients were admitted for malignant disease, though none of them had a kidney tumour or any clinical evidence of kidney dysfunction. The values for standard clearance ranged from 16.60 c.c. to 51.30 c.c. with an average of 35.16 c.c. These values appeared to indicate an impaired kidney function on the basis of standards suggested by Möller *et al.* for Americans, but normal function on the basis of standards for Indians suggested by Gokhale and by Srikantha and Shamanna. The implications of these differences have been discussed and the need for collection of further data for normal standards in Indians has been advocated.

10. OBSERVATIONS ON THE PHYSIOLOGICALLY ACTIVE FRACTION OF INDIAN HEMP, *Cannabis sativa* LINN.

A comparative pharmacological study of the alkali-soluble and alkali-insoluble fractions of *charas* in CCl₄ and petrol-ether solvents has been made. The total extract and the alkali-insoluble fraction were found

to possess the narcotic properties of the drug as evidenced by the production of ataxia in cats. The alkali-soluble fractions were found to be devoid of all physiological activities. Most of the chemical and colorimetric tests including the test recently described by Mukhopadhyaya *et al.* depending on the presence of phenols in the alkali-soluble portion of the CCl₄ extract, do not measure the narcotic potency of hemp drugs. A comparison of the action of homotetrahydrocannabinol and the alkali-insoluble fraction of *charas* shows that the former or an allied compound is possibly the active principle for the narcotic effect of hemp. The activity of the alkali-insoluble portion of hemp resin is greater than that of homotetrahydrocannabinol. This suggests that the alkali-insoluble portion probably contains some optical isomers of tetrahydrocannabinol which are more active than tetrahydrocannabinol or its optically inactive homologues.

11. ANÆMIA IN INDIAN ARMY RECRUITS

The hæmoglobin, red cell count, and packed cell volume of some 600 newly joined Indian army recruits were estimated. Most of these men were drawn from the labouring classes, and 25 to 40 per cent of different races had less than 13 g. hæmoglobin. The nursing sepoy recruits were drawn from a higher social class than other recruits, and only 8 per cent had less than 13 g. hæmoglobin. Most of the anæmia was normocytic and normochromic, but every type was found. Macrocytic anæmia was rare. The anæmia of U. P. recruits differed from that of Punjabis and Madrasis. Hookworm infestation was an important contributory cause of the anæmia, but it was often not present in even the severer anæmias, and many infested men were not anæmic. The anæmia of these recruits improved considerably during the first 3 months of training, but progress then stopped and much anæmia remained incompletely cured. When a daily dose of 6 grains ferrous sulphate was given the progress was much more rapid, and even after 3 months most anæmic men were cured.

12. CULTIVATION OF A PROTOZOAL PARASITE OF THE CENTRAL NERVOUS SYSTEM *in vitro* AND ITS RELATIONSHIP TO RABIES

A simple medium containing sheep-brain extract, sheep serum and fresh young guinea-pig brain has been described for the *in vitro* cultivation of the protozoal parasite of the central nervous system previously described by the author. The morphological appearances of the parasite and the method of multiplication *in vivo* and *in vitro* are those of a protozoan. Cultures showing the presence of the parasite were found to be infective in much higher dilution than the original inoculum. The parasite has never been encountered in the brains of normal guinea-pigs, rabbits, sheep and dogs, or in cultures of them. The parasite has been observed regularly in cultures inoculated with the Paris strain of rabies, fixed virus and with all of the strains of rabies street virus so far investigated. Filtration experiments with Berkefeld V and N candles have been described; these experiments indicate that certain stages in the development of the parasite in cultures are 'filtrable'. These findings provide further evidence in support of the view that the protozoal parasite described is connected with the ætiology of rabies.

13. A RAPID METHOD FOR THE DIAGNOSIS OF RABIES IN ANIMALS

A rapid and delicate method for the diagnosis of rabies in animals is described.

14. THE SUSCEPTIBILITY OF INDIANS TO CANCER

A study of the clinical material from medical institutions in India, as well as a guarded use of official statistics suggests that Indians are as liable to suffer from cancer as the inhabitants of Western countries. Evidence has been presented to show that though the total incidence of cancer in several countries may show small differences, the incidence of cancer in various parts of the body is markedly different in different peoples. The implications arising out of these findings are briefly discussed.

Treatment of Diabetic Acidosis and Diabetic Coma

By T. P. ALMY, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 24th November, 1945, p. 849)

METHOD OF TREATMENT

INTERNS are instructed to treat diabetic acidosis and diabetic coma as follows:—

1. As soon as the diagnosis is made, give 25 units of regular insulin subcutaneously and repeat this every half-hour until the patient is free from all signs of ketosis, as judged by clinical and laboratory evidence.

2. When possible, replacements of fluid, salt and carbohydrate should be given by mouth. Give in each hour (a) 50 to 75 gm. of glucose as orange juice (500–750 c.c.), grape juice (300–450 c.c.) or fortified fruit juices; (b) salty broth, 200 c.c.; (c) enough water to make the total fluid intake 1,000–1,500 c.c.

3. If the patient is drowsy or comatose, or if the patient has vomited or has been nauseated during the preceding twenty-four hours, therapy must be begun by the intravenous route: (a) Infusion of 5 per cent glucose in isotonic solution of sodium chloride, which should run in at first at the rate of 750–1,000 c.c. per hour. (b) The rate of this infusion should be reduced as soon as dehydration is relieved. Patients over 40 years of age, any with notable arteriosclerosis and any with cardiovascular disease, may have to be infused at slower rates and should be observed frequently and with extreme care for signs of increased venous pressure and passive congestion of the lungs.

Return to the oral route as soon as the patient is fully conscious and free from nausea.

4. Test a urine specimen every half-hour or every hour for sugar, acetone and diacetic acid. (Catheterize if necessary.) Continue the foregoing therapy until the urine is free from acetone and diacetic acid. Do not leave the ward until this is accomplished.

5. When ketonuria and all clinical signs of acidosis have disappeared, give fruit juice and 25 units of insulin at two-hour intervals for at least eight more hours.

6. If the patient is anuric, guide the therapy by frequent estimations of the carbon dioxide combining power of the blood. This rule will also apply if acidosis should occur without the presence of acetone bodies in the urine. (Such cases are exceedingly rare and have not yet occurred in our experience.)

Every patient whose urine contains sugar and acetone bodies is treated thus, regardless of the severity of the diabetic acidosis. Many of the milder cases so treated have been excluded from the series reported here, but no fatal case has been excluded, nor any in which the acidosis did not promptly respond to treatment.

The fundamental disturbance in diabetic acidosis is a depletion of water, sodium and glucose in association with a relative insufficiency of insulin.

There is general agreement that the most important step in the therapy of acidosis is the use of large quantities of insulin, and to this we subscribe. There is likewise general recognition of the need for restoring water and sodium ion, and in all clinics the patients receive water and sodium chloride, by vein if necessary. Sodium chloride is useful for relieving acidosis only if the kidney is capable of excreting the chloride in combination with ammonium ion, the sodium being retained as base. If the kidney is insufficient, most will agree that it is better to supply sodium as sodium lactate or sodium bicarbonate.

There has been disagreement concerning the use of glucose in the treatment of diabetic acidosis and diabetic coma. The state of depletion of carbohydrate in the body in diabetic coma has not generally been recognized because the blood, the only tissue tested under such circumstances, always shows an excessive concentration of sugar. That there is truly a state of depletion of carbohydrate in the body in coma is

attested by the figures of Soskin, although these figures are contested by Root.

Among 99 cases of diabetic acidosis and diabetic coma so treated during the past five years there were 7 deaths, only 1 of which was due to diabetic acidosis per se. In that patient there was proved insulin resistance of a high order.

CONCLUSION

Our experience indicates that patients with diabetic acidosis or diabetic coma can be successfully treated with small, standard and frequently repeated doses of insulin, that the administration of glucose in this disorder is beneficial and not harmful, that it is not necessary to follow the blood sugar and carbon dioxide combining power as guides to therapy, and that with such a simple method the constant attendance of specialists in diabetes mellitus is, in all but rare instances, unnecessary.

Early Rising in the Puerperium

By G. ROSENBLUM, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 24th November, 1945, p. 849)

Our data indicate that delivered women can safely and advantageously get up early in the puerperium with no harmful results occurring.

Bowel function particularly is improved as a result of early rising in the puerperium.

Early puerperal rising reduces the amount of nursing care required.

The majority of patients managed in this way reported favourably on the method.

The statistics show no particular advantage to third or fourth day puerperal rising as compared to the earlier first and second day figures.

It is our opinion that early rising results in more rapid and comfortable convalescence, with less asthenia and less postoperative and postpartum depression.

It is our hope that this study will encourage further interest and continued observation on the question of early puerperal rising which may eventually clarify this still unsettled problem.

Promin in Pulmonary Tuberculosis: A Progress Report

By R. J. DANCEY, *et al.*

(From the *American Review of Tuberculosis*, Vol. XLIX, June 1944, p. 510. As abstracted in the *Bulletin of Hygiene*, Vol. XX, June 1945, p. 310)

(Continued from November 1945 issue of the *I.M.G.*)

Toxic effects are tabulated for 32 cases treated orally, showing anaemia in all, cyanosis in 30, gastrointestinal symptoms in 17, headache in 11, and, among other conditions, jaundice in 8, skin rash in 4, and leucopenia, fever, and lower limb paresis, 1 each.

Hæmoglobin fell by 15 to 32 per cent of normal in 21 cases, and by 6 to 15 per cent in 11. A fairly steady maintenance level of 60 to 80 per cent was reached in 25.

For the 16 cases, three of moderately and 13 of far advanced disease, therapeutic results are classed as marked improvement in five, moderate improvement in four, slight improvement in four, no change in two, and 'slight an improvement' (apparently slight progression of disease) in two. Cavity closure was rare, and sputum conversion occurred in only two cases.

It is concluded that promin is not a very potent curative agent in human pulmonary tuberculosis, and it is doubtful whether higher dosage would have improved the results, since the blood levels were of the same order as those giving curative effects in the guinea-pig. Promin should not be expected to replace accepted forms of treatment, but is a possibly addition.

Muscle Hernia

By MAJOR H. E. SIMON

(Abstracted from the *Military Surgeon*, Vol. XCVII, November 1945, p. 369)

OCCURRENCE

MUSCLE hernia or the protrusion of muscle tissue through a defect in the overlying fascia is recognized with extreme rarity in civilian life. In military service it is frequently observed and often symptomatic.

CLINICAL FINDINGS

It may appear in any portion of the body in which fascia overlies muscle, the tibialis anticus being most often involved. The hernia appears as a circumscribed semifluctuant swelling which varies in size or disappears depending upon the position of the part involved and the state of contraction of the underlying muscle. Typically when the involved part is elevated or coincident with contraction of the underlying muscle the swelling decreases in size or disappears but it increases in size with muscle relaxation. The swelling is reducible by pressure revealing a circumscribed defect palpable in the fascia. Aching pain or local tenderness is often present.

The hernias due to direct trauma appear immediately or several months after resumption of muscular activity following an ætiologic accident such as fracture, contusion, laceration or puncture. These may occur in any location but most often in the leg or forearm. They are typically solitary.

Those due to indirect trauma such as the sudden stoppage of a powerful muscular contraction as in bowling, occur most often in the thigh. Their appearance is abrupt after the accident.

The idiopathic type is usually small, not infrequently multiple or bilateral and occurs almost exclusively in the legs. Their onset is gradual and they are found usually after the individual has engaged for some time in increased muscular activity such as mountain climbing, wrestling or drilling.

The small hernias in particular may be mistaken for a localized varicosity and may be unrecognized even after unsuccessful aspiration. A rupture of a muscle, localized mass of varicosities, angioma, arterio-venous aneurism, lipoma, myoma, cyst or other localized tumour may be confused with muscle hernia but the characteristic reduction of the latter coincident with elevation of the involved part, enlargement with relaxation of the underlying muscle and the characteristic palpable fascial defect makes his diagnosis evident if the condition is borne in mind.

TREATMENT

The majority of muscle hernias require no treatment because of absence or mildness of symptoms. When the defects are large and deforming or symptoms are sufficient to interfere with normal activities and it is established that the symptoms result from the hernia and not from co-existing defects, then treatment is indicated.

Temporary symptomatic relief may be obtained by elastic pressure bandages which may also be used as a therapeutic test for the relationship between symptoms and hernia. Temporary improvement has been reported following injection of sclerosing solutions such as sodium morrhuate: in some instances reduction in physical activities is all that is necessary to relieve symptoms.

For permanent cure surgical treatment is usually necessary. The simplest surgical procedure consists of careful exposure of the fascial defect and closure by overlapping and suture of the fascial edges taking care to preserve nerves or important blood vessels that emerge through it. The use of a strip of fascia as a suture to close these small hernias would seem ideal. When the defect is large or rigidity of the fascia prevents its approximation without undue tension the procedure of choice is repair by fascia transplant either in the form of a patch or interlacing strips.

Hæmorrhage from Puncture Biopsy of the Liver

(From the *Journal of the American Medical Association*, Vol. CXXIX, 3rd November, 1945, p. 680)

ONE great danger of biopsy of the liver, now practised extensively by aspiration, is hæmorrhage from the puncture. According to Raby 7 instances of fatal hæmorrhage have been reported, all in advanced or severe cases of carcinoma or pernicious anæmia. Vitamin K was not given in any case before the puncture. The coagulation time was determined beforehand in only 1 case, and here clotting was delayed. Raby himself reports in detail a fatal intraperitoneal hæmorrhage from puncture of a portal branch near the anterior surface of the right lobe of the liver in a woman aged 79 with jaundice of uncertain origin. The coagulation time before puncture was normal. The patient died thirty-six hours after the biopsy in spite of hæmostatic treatment and blood transfusion. Raby also reports the death of a man aged 85 with senile dementia but without any hæmorrhagic tendencies, which occurred three days after biopsy of the liver. The symptoms seemed obscure and post mortem did not reveal any primary cause of death. Bacteriologic examination was not made. Clearly, puncture of the liver is not without danger, especially in old persons. Precautions should never be neglected when puncture is indicated, hæmorrhagic tendencies should be excluded. Raby recommends also that the patient's blood group be determined before puncture and that the patient be watched closely after the puncture in order that transfusions may be made if necessary without delay.

Reviews

SKIN GRAFTING OF BURNS.—By James Barrett Brown, M.D., and Frank McDowell, M.D. 1943. J. B. Lippincott Company, London. Pp. xi plus 204, with 131 illustrations

THIS book outlines the essential points of care which have proved of benefit in treating a large series of patients with full-thickness loss of skin and requiring skin grafting, at the Washington University Medical School Children's Hospital and Barnes Hospital, during the course of a long period. In the first chapter, the authors state: 'In the extensive literature on burns, there has been a notable lack of reports of completed cases, i.e. final demonstrations of patients who have been badly burned and who have not only been treated and saved from death but who have had complete, final, and satisfactory surgical repair of resultant open wounds and contractures. Apparently most effort has been devoted to the development of some single method of caring for the local area, and of taking care of the acute stage of shock. Seemingly the wounds are allowed to heal as they will, or the final outcome—functional and cosmetic—is not reported'. The sixteen chapters of the book, and particularly the excellent illustrations contained in them, have greatly remedied the defect pointed above. A preliminary survey of the subject is given in the first chapter. Early general and local care is dealt with in two chapters, and spontaneous healing of burns in the fourth chapter. Seven chapters deal with the various aspects of skin grafting such as preparation of wounds, varieties of skin grafts, application of thick split skin and free full-thickness grafts, pedicle flaps, homografts, and faults of skin grafts. One chapter deals with contractures. Regional repairs of trunk and extremities and head and neck are discussed in two chapters, and final results in burned patients in one chapter. The final chapter on treatment of burns in World War II was written by one of the authors while on active service in the European

theatre of operations. The book is direct and practical, and the text matter is brief but substantial.

J. L.

THE SYMPTOMATIC DIAGNOSIS AND TREATMENT OF GYNÆCOLOGICAL DISORDERS.—By M. Moore White, M.D. (Lond.), F.R.C.S. (Eng.), M.R.C.O.G. Second Edition. 1946. H. K. Lewis and Company, Limited, London. Pp. x plus 246, with 108 illustrations. Price, 16s.

It is stated in the foreword, 'that of gynæcological textbooks there is no dearth'.

This is of course true, and it is also a fact that more are published year by year, some as is natural being better than others.

Miss Moore White's little book is certainly one of the better ones, and a fact that a second edition was called for only a little over two years since the appearance of the first is evidence of its worth.

This edition is noteworthy in that it contains a good thorough brief account of penicillin therapy in the treatment of gonorrhœa.

Special mention must also be made of the chapter which deals with contraceptive methods. In it is detailed in clear and easily understood phraseology the advice which is so often earnestly required but so frequently is but too briefly given.

The book is well printed, and the diagrams are clear and decisive.

There appears to be a pictorial error in the first diagram as the left lateral position is described as the Sims'.

Every general practitioner who has gynæcological patients is advised to obtain this volume.

H. E. M.

CLINICAL PATHOLOGY.—By P. N. Pantou, M.A., M.B., B.Chir. (Cantab.), and J. R. Marrack, M.A., M.D. (Cantab.). With the assistance of H. B. May, M.A., M.D. (Cantab.), M.R.C.P. (Lond.). Fifth Edition. 1945. J. and A. Churchill Limited, London. Pp. x plus 450, with 12 plates (10 coloured) and 45 illustrations in the text. Price, 21s.

This book has undergone many changes in this edition and includes the description of many new methods, particularly in hæmatology and chemical pathology. A new section on antibacterial chemotherapeutic substances with details of the common laboratory methods used in the control of treatment with sulphonamide drugs and penicillin has been added. The book describes laboratory investigations and have a practical bearing in the diagnosis and treatment of disease and should be an useful guide to practitioners in their daily work.

R. N. C.

THE ELEMENTS OF MEDICAL TREATMENT.—By Sir Robert Hutchison, Bart., M.D., D.Sc., LL.D., F.R.C.P. Fourth Edition. 1945. John Wright and Sons Limited, Bristol. Pp. 213. Price (not stated)

ALTHOUGH completely revised, this book retains its original character, viz, discussion of the elementary principles of treatment and their application to the commoner forms of disease met with in practice. It is 'largely designed to instruct the student in the fast disappearing art of prescribing'. Emphasis is put on treating the patient and not the disease, cautious adoption of new and up-to-date methods unless they have been proved useful, and avoidance of arbitrariness in prescribing diet. The book is meant for students, but many young doctors will also profit by it.

R. N. C.

TREATMENT IN GENERAL PRACTICE.—By Harry Beckman, M.D. Fifth Edition. 1945. W. B. Saunders Company, Philadelphia and London. Pp. xiii plus 1070. Price, 50s.

A PERUSAL of this book shows that great care has been taken to revise it and presents up-to-date and reliable information on treatment—no mean feat in war time. It deals chiefly with medical diseases, but also includes common skin diseases and some gynæcological disorders which are common in general practice. There are chapters on acute poisoning, burns and shock, and the last one deals with toxic and other special features of sulphonamide therapy. Several new entities have been added in this edition, but it is a pity that five major infectious diseases, viz, cholera, leprosy, plague, trypanosomiasis and yellow fever, have been omitted; this is because in the U.S.A. the management of these diseases has been taken over by public health authorities or other specialists, and does not concern the general practitioner. The general plan of the book is to briefly discuss the general features of a disease and then pass on to therapeutics. Various modes of treatment are accurately presented and fairly assessed. Some common but important diseases have been liberally dealt with, e.g. common cold, malaria, pneumonia, rheumatic affections, syphilis, tuberculosis, typhoid and paratyphoid fevers and diabetes. The reading is easy and pleasant and enlivened by the author's frank remarks and observations. The book maintains the high standard of previous editions.

R. N. C.

PRACTITIONER AND INTERNS HANDBOOK.—By Members of the Faculty of the College of Medicine, Syracuse University. Under the direction of M. S. Dooley, A.B., M.D., and M. E. Holmes, M.D., F.A.C.P. Third Edition. Second Impression. 1945. J. B. Lippincott Company, Philadelphia and London. Pp. xvii plus 579. Illustrated. Price, 21s.

ORIGINALLY meant for the interns only, the present edition of the book will prove equally, if not more, useful to the practitioner.

The size has increased but every word is readable. The Committee have not allowed 'the thought to stand in its own way hindered by words that weigh down the tired ear'. The price has also increased. It is an excellent handbook which gives up-to-date information to the general practitioner on all items.

An obvious error occurs in the note on penicillin on page 511: In the first paragraph the list should end with item (6).

The paper, printing (apart from faulty margin on pp. 490, 497, 500, 501, 520, 521, 524 and 525) and binding are good. No printer's errors attract attention.

S. D. S. G.

A NEW CONCEPTION OF KERATOCONJUNCTIVITIS SICCA.—By Henrik Sjögren. Translated by J. Bruce Hamilton. 1943. Australian Medical Publishing Company, Limited, Sydney. Pp. 152, with 56 illustrations

THIS monograph, originally published in Sweden in 1933, has been translated into English.

The disease Keratoconjunctivitis Sicca also known as 'filamentary keratitis' or 'Sjögren's syndrome' is one of considerable rarity. In this book nineteen cases are recorded. It occurs almost always in middle-aged women, runs a chronic course and is incurable. Symptoms are itching, burning and photophobia, and a feeling of foreign body in the eyes. The disease is almost always bilateral. Dryness of the eyes and scantiness of tears and also dryness of the mouth are sometimes noticed.

Examination reveals a little tenacious conjunctival secretion and on the surface of the cornea are seen multiple filaments of eroded epithelium. These are usually very narrow and only about 2 mm. long. The remaining portions of the eye are normal as is also

the corneal sensitivity. Visual acuity is slightly diminished. In all cases the lachrymal secretion is diminished and in some the complaint is made of diminished salivation. The disease in many cases is also associated with arthritis.

The monograph contains excellent photographs of the histological findings—epithelial erosions of the cornea and chronic inflammatory and fibrotic changes in the lachrymal glands. Dr. Hamilton has added an appendix on possible lines of treatment. A bibliography is appended.

E. J. S.

MURRELL'S WHAT TO DO IN CASES OF POISONING.—By Harold G. Broadbridge, M.B., B.S. (Lond.). 1944. Fifteenth Edition. H. K. Lewis and Company, Limited, London. Pp. 190. Price, 8s.

TIME has placed a halo of honour round this little book first published in 1881. It gives to-day, as it gave then, all that can be done in a case of poisoning.

The use of stomach tube has been encouraged even in the case of corrosive poisons. If the gullet and the stomach have perished before the arrival of the medical man the patient is going to die in any case. Doubt has been cast on the efficacy of ferric hydroxide as an antidote in arsenic poisoning. That should remove the compound from the important position of an ingredient of the Universal Antidote also.

Two items need amendment in the next edition: (1) Wasp stings are now treated with vinegar. (2) Cauterization and potassium permanganate have no longer a place in snake-bite—the latter can only be used as a mouth wash for the person who sucks the wound. Scorpion sting may be included for the practitioners in the tropics. An obvious omission on page 14 (item XXI, line 5) may be supplied.

The get-up of the book is excellent and the size particularly suitable for the emergency bag.

S. D. S. G.

DISEASES OF THE NOSE, THROAT AND EAR.—By I. Simson Hall, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E. Third Edition. 1944. E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 439, with 82 figures including 8 coloured plates. Price, 15s. net

EVERY medical practitioner should be familiar with the common diseases of the ear, nose and throat which constitute a considerable part of general practice. This book is an excellent source of knowledge on these diseases, and gives a sufficient and clear description of the commoner diseases of nose, throat and ear. As regards surgical treatment of these conditions and technique, the guidance given is based upon the author's course of lectures to students. The sections on the nose, nasal sinuses, the pharynx, the larynx, and the ear, first contain a short anatomical description of the part. Endoscopy is dealt with separately in a short section.

The book is well illustrated, some of the illustrations being in colour. The paper used is of high quality and the printing is in bold type.

J. L.

THE PROBLEM OF LUPUS VULGARIS.—By Robert Aitken, M.D., F.R.C.P.E., F.R.S.E. 1946. E. and S. Livingstone, Limited, Edinburgh. Pp. viii plus 69. Illustrated. Price, 15s.; postage, 7d. (Home)

THIS little book is well written, and the author has put before the public health authorities and the medical practitioners of his country the problem of the disease and his suggestions and recommendations for dealing with it.

The clinical features of the disease have been well illustrated by coloured plates and the lines of treatment given are brief, clear cut and impressive—the result of the author's long experience.

It is hoped that the author's labour will arouse interest amongst the public, physicians in general and the health authorities in this matter.

The publishers are to be congratulated for the get-up of the book and the striking plates.

L. M. G.

PENICILLIN THERAPY.—By J. R. Goyal, M.B., B.S. 1945. Printed and Published by B. Datta, Esqr., Manager, The Albion Press, Kashmir Gate, Delhi. Pp. 148. Price, Rs. 5. Available from the 'Medical Review of Reviews', Burn Bastion Road, Post Box No. 160, Delhi

In the preface Dr. Goyal says that his object in writing this book is to give a concise authentic account of penicillin by collecting all the data that are available on the subject. There is at first given a description of pharmacology and therapeutics, and then follow several chapters on its uses in various infections. The information given is, on the whole, accurate, but we may offer some comments. The book has been written in the form of a compilation embodying the various results obtained by different workers with little or no attempt to correlate them; this is not likely to be very helpful to a busy practitioner. Indian parents are not likely to consent to three-hourly injections to their new-born babies for ophthalmic neonatorum; on the other hand, nothing is said about frequent local instillations which appear to give equally good results. There is no mention of the fact that penicillin treatment of gonorrhoea may mask the symptoms of co-existing syphilitic infection. The value of the drug in tetanus has not yet been proved, yet one may be led to believe in its efficacy on the basis of two cases which had received anti-toxin and sedatives as well. There was no special need to include tularæmia and rheumatoid arthritis, if penicillin had no effect on them. We hope it will be possible to remedy these including several misprints in the next edition and thereby enhance the value of the book.

R. N. C.

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL D. V. O'MALLEY, O.B.E., V.H.S., is appointed Honorary Surgeon to The King, 19th June, 1945, Colonel B. C. Ashton, C.B.E., deceased.

Colonel R. N. Khosla, O.B.E., is appointed Honorary Surgeon to The King, dated 12th July, 1945, *vice* Major-General H. J. M. Cursetjee, C.S.I., D.S.O., retired.

The Viceroy and Governor-General has been pleased to make the following appointments on His Excellency's personal staff:—

To be Honorary Surgeon

Colonel D. Clyde, C.I.E., dated 23rd August, 1945, *vice* Colonel A. H. Harty, C.I.E., vacated.

Lieutenant-Colonel T. S. Shastri, I.M.S. (Retd.), has been appointed as Director, Government of India Medical Relief Parties (Malaya), with effect from the 12th January, 1946 (forenoon).

Major H. B. Wright, Deputy Assistant Director-General, Medical Store Depot, Madras, is appointed to officiate as Assistant Director-General, Indian Medical Service (Stores), with effect from the 12th January, 1946, *vice* Major B. A. Porritt, granted leave.

Major V. Srinivasan on reversion from military duty was placed on special duty in the Office of the Inspector-General of Civil Hospitals, Central Provinces and Berar, from 21st January, 1946 to 23rd January, 1946 (both days inclusive), and then assumed charge as Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, from the 24th January, 1946.

Lieutenant-Colonel E. C. Hicks is appointed as Medical Adviser (Pensions) in the War Department, 30th January, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

William Hayes. Dated 19th April, 1945.

Anil Kumar Guin. Dated 13th September, 1945.

Cuppam Mohan Rangam. Dated 14th September, 1945.

Suresh Kumar Varma. Dated 15th September, 1945.

To be Lieutenants

Rajindra Lal Chopra. Dated 10th February, 1945.

Iqbal Singh. Dated 10th February, 1945.

Cornelius Patrick O'Flynn. Dated 25th May, 1945.
11th September, 1945

Bal Krishnan Jerath. Anamtapally Visweswara.
13th September, 1945

Rathindra Nath Datta. John F. Gow.

Richard Mark Gueizelar. Arthur Lambart Scaley.

Ram Chandra. Dated 15th September, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY DENTAL CORPS
(DENTAL BRANCH)

(Emergency Commission)

Ram Pratab. Dated 30th December, 1943.

LEAVE

Major B. A. Porritt, Assistant Director-General, Indian Medical Service (Stores), is granted leave on average pay *ex-India* for 8 months, with effect from the 11th January, 1946.

PROMOTIONS

INDIAN MEDICAL SERVICE

To be Major-General

Colonel W. R. Stewart, C.B., C.I.E. Dated 12th July, 1945.

Lieutenant-Colonels to be Colonels

J. R. Kochhar. Dated 20th June, 1945.

S. M. A. Faruki. Dated 12th July, 1945.

Majors to be Lieutenant-Colonels

W. A. Burki, C.B.E. Dated 10th November, 1945.

T. B. Pahlajani. Dated 15th December, 1945.

Captains to be Majors

B. M. Wheeler. Dated 31st October, 1945.

E. H. Wallace. Dated 27th December, 1945.

J. E. O'Donnell. Dated 28th December, 1945.

INDIAN LAND FORCES—INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captains to be Majors

Y. K. C. Pandit. Dated 26th June, 1945.

M. R. Vasuna. Dated 1st August, 1945.

1st September, 1945

B. L. Kamra. N. Ahmad.

15th October, 1945

B. M. Sinha. V. Rangachari, M.C.

S. N. Sinha.

M. A. M. Chaudhry. Dated 16th October, 1945.

J. Jacob. Dated 17th October, 1945.

S. C. Chatterjee. Dated 18th October, 1945.

B. Mukerji. Dated 20th October, 1945.

1st November, 1945

V. S. Iyer. S. B. Singh.

M. Mamen. Dated 2nd November, 1945.

5th November, 1945

T. K. Chary. D. T. Gandhi.

V. K. Viadyer. Dated 6th November, 1945.

M. V. Ramanamurti. Dated 13th November, 1945.

15th November, 1945

R. C. D. Tarapora. S. B. Lal.

B. S. R. Waglay.

T. R. A. V. Nath. Dated 18th November, 1945.

M. R. Vachha. Dated 20th November, 1945.

K. S. Pillai. Dated 26th November, 1945.

2nd December, 1945

P. F. D'Souza. K. S. M. B. Menon.

I. K. Kar. V. G. Parda.

M. N. Sen.

N. T. Ghaisas. Dated 3rd December, 1945.

P. M. Bhandarkar. Dated 10th December, 1945.

N. C. Sekhar. Dated 12th December, 1945.

M. B. Chakrabarty. Dated 16th December, 1945.

N. Dutt. Dated 29th December, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captains to be Majors

N. G. Gadakar. Dated 20th October, 1945.

M. Ibrahim. Dated 1st November, 1945.

V. S. Ramaswami. Dated 5th November, 1945.

H. C. Duncan. Dated 6th November, 1945.

H. Chapman. Dated 8th November, 1945.

K. K. Seal. Dated 15th November, 1945.

J. G. Bentley. Dated 30th November, 1945.

C. M. Burnio. Dated 18th December, 1945.

S. A. Hasan. Dated 22nd December, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
(Emergency Commissions)

Lieutenants to be Captains

J. P. Zachariah. Dated 7th February, 1941.

D. C. Lagan. Dated 5th March, 1942.

H. R. S. Harley. Dated 5th March, 1942.

(Mrs.) M. E. M. Napier (Nee Fleming). Dated 29th July, 1942.

T. Singh. Dated 12th July, 1945.

B. D. Tiwari. Dated 22nd September, 1945.

P. Dorai Raj. Dated 31st October, 1945.

K. Gokhale. Dated 7th November, 1945.

8th November, 1945

Mushtaq Ahmad Chaudhri. S. Rashid-ul-Hamid.

I. S. Dhingra. Dated 9th November, 1945.

10th November, 1945

A. D. Salah-ud-Din. J. K. Sahgal.

M. H. Arbab. Dated 16th November, 1945.

S. K. Gupta. Dated 24th November, 1945.

D. M. Markar. Dated 5th December, 1945.

H. L. Dutta. Dated 9th December, 1945.

V. D. Paliwal. Dated 10th December, 1945.

M. H. Khan. Dated 14th December, 1945.

J. C. Karamkar. Dated 18th December, 1945.

G. D. Dhavla. Dated 19th December, 1945.

S. S. Digha. Dated 21st December, 1945.

H. S. Athwal. Dated 27th December, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Lieutenants to be Captains

R. L. Chopra. Dated 23rd April, 1945.

C. P. O'Flynn. Dated 14th June, 1945.

T. Singh. Dated 12th July, 1945.

A. B. Ray. Dated 3rd September, 1945.

B. N. Bardhan. Dated 8th September, 1945.

S. S. Dhanoa. Dated 11th September, 1945.

Iqbal Singh. Dated 6th October, 1945.

8th October, 1945

P. L. Chatterjee. M. N. Chengappa.

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY
(Emergency Commissions)

Lieutenants to be Captains

10th November, 1945

K. S. Isar.

N. Nizami.

M. P. Bhalla.

Mahammad Anwar
Choudhrie.

B. C. Bhail. Dated 11th November, 1945.

G. H. Pirzada. Dated 23rd November, 1945.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Miss) G. S. Singh. Dated 15th October, 1945.

(Miss) A. Kallat. Dated 23rd October, 1945.

RELINQUISHMENTS

Captain Ramchandra Dattatraya Marathe, 26th January, 1946, and is granted the honorary rank of Captain.

Captain C. H. Cousins, 8th February, 1946, and is granted the honorary rank of Captain.

The undermentioned officer is permitted to relinquish her commission on grounds of ill health :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)
(WOMEN'S BRANCH)

Captain (Miss) M. M. Shrinagesh, 29th January, 1946, and is granted the honorary rank of Captain.

(WOMEN'S WING)—British

Captain (Mrs.) E. C. Just, 27th December, 1945, and is granted the honorary rank of Captain.

The undermentioned officers are permitted to relinquish their commissions on release from the army service and are granted honorary ranks of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major G. R. Charnalia. Dated 2nd November, 1945.
Major Shiva Chandra Banerjee. Dated 29th November, 1945.

Major J. N. J. Pachcho, 18th December, 1945, and is granted the honorary rank of Major.

Major Sarveshwar Nath Kaul, 30th December, 1945, and is granted the honorary rank of Major.

The undermentioned officers are permitted to relinquish their commissions on release from army service :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major G. K. Mitra, 16th December, 1945, and is granted the honorary rank of Major.

Major J. S. P. Coutts, 24th December, 1945, and is granted the honorary rank of Major.

Major M. K. K. Menon, 28th December, 1945, and is granted the honorary rank of Lieutenant-Colonel.

Major A. L. Sutherland, 3rd January, 1946, and is granted the honorary rank of Major.

Major E. J. Ramdas, 11th January, 1946, and is granted the honorary rank of Major.

Major Jyotsnananda Sen, 11th January, 1946, and is granted the honorary rank of Major.

Major S. Ganeswaran, 30th January, 1946, and is granted the honorary rank of Major.

Captain Nibaran Chandra Ghosh, 30th January, 1946, and is granted the honorary rank of Captain.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain K. S. Rau. Dated 3rd November, 1945.

The undermentioned officers are permitted to relinquish their commissions :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain Hamid Shafi Qazi, on grounds of ill health, and is granted the honorary rank of Captain, 16th November, 1945.

Captain Satya Pal, 26th November, 1945, and is granted the honorary rank of Captain.

Captain Rustum Bomanji Daruvala, 27th December, 1945, and is granted the honorary rank of Captain.

The undermentioned officer is permitted to relinquish his commission on grounds of ill health :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain S. Subramanian, 3rd January, 1946, and is granted the honorary rank of Captain.

Captain C. R. Iyengar, 4th January, 1946, and is granted the honorary rank of Captain.

Captain K. R. Unger, 6th January, 1946, and is granted the honorary rank of Captain.

Captain F. W. Perreira, 9th January, 1946, and is granted the honorary rank of Captain.

Captain K. M. Rowther, 25th January, 1946, and is granted the honorary rank of Captain.

The undermentioned officers are permitted to relinquish their commissions on release from army service :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)—Specialists

Captain (A/Col.) Chitra Kanaka Prasada Rao, 13th January, 1946, and is granted the honorary rank of Lieutenant-Colonel.

RETIREMENTS

Major-General W. C. Paton, C.I.E., M.C. Dated 23rd August, 1945.

Lieutenant-Colonel G. B. Hanna, O.B.E., retires on account of ill health. Dated 3rd October, 1945.

Lieutenant-Colonel B. B. Gadgil. Dated 16th January, 1946.

RESIGNATION

The undermentioned officer is permitted to resign his commission :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain J. F. Paas, 20th November, 1945, and is granted the honorary rank of Captain.

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Original Articles

THE ACTION OF NICOTINIC ACID ON THE HEART OF *RANA TIGRINA*

By S. H. ZAIDI, M.D.

Physiological Laboratory, Lucknow

THE views regarding the action of nicotinic acid on the blood vascular system are still divided. All the workers agree that there is a definite action; the exact significance, however, is still doubtful. Loman *et al.* (1941) has demonstrated that the main action is that of peripheral vasodilatation and that there is no independent significant change in the blood pressure.

My own experiments have been carried out on the hearts of *Rana tigrina* and they confirm in part only the results of other workers. Besides, I have been able to discover certain new facts by the use of a much wider range of concentrations of the drug, as advocated by Burridge (1935).

Method.—The hearts were perfused *in situ* with Ringer's solution having various gradations of calcium. Those having low calcium were termed R/10 and R/5 indicating that the calcium content was 1/10th and 1/5th of the normal so-called balanced Ringer's solution.

The dilutions used ranged from 1 : 1,000 to 1 : 10,000,000,000.

My results show that nicotinic acid exerts two independent actions on the heart, the one a depressor action exerted only by high concentrations, and the other a stimulating action. The latter is only observed with dilute solutions of nicotinic acid.

The nicotinic acid used was made by Messrs. Eli Lilly International Corporation, U.S.A.

Results.—The first tracing illustrates the action of a one in one thousand solution of nicotinic acid on the hearts perfused as described (see figure 1, plate XVII).

The nicotinic acid solution was perfused at the arrow marked Ni 10^{-3} . The base line whence the contractions start is seen to rise before the arrow and fall again afterwards. The rise and the fall were caused by the perfusion pressure changes consequent on the use of a one-way cannula. The rise commenced when the perfusion ceased as the rubber tube from the reservoir of Ringer's solution was disconnected. The fall began when the nicotinic acid-Ringer reservoir was connected. The commencements of rise and fall thus accurately mark the changes made. This pressure fall subsequently merges into a real fall of beats due to the action of the drug.

The subsequent beats fall down to the extent that the heart is finally arrested in diastole.

At the arrow R/10 the perfusion of Ringer's solution was resumed. It is observed that the

arrested heart gradually and steadily recovers. Each succeeding beat becomes more and more powerful finally resulting in the circus movements of the ventricle. The circus movements, themselves short-lived, were followed by more defined beats firstly only ventricular and finally both auricular and ventricular. The heart first regained its original amplitude and then it started beating with renewed strength with the result that the amplitude increased by about 50 per cent and also there was an increase in 'tone' since the contractions were away from the base line (Burridge, 1935). There was squirting of the fluid coming out of the ventricle. Ordinarily, the fluid coming out through the slit in the ventricle just oozes out and bathes the heart, while in the case in question the fluid was squirted out as if coming from a jet. It was being expelled not only at a greater rate but also the quantity was greater as roughly estimated from too frequent charges of the reservoir flask. The amount was definitely doubled and at times trebled.

The recovery of the heart after the depression is noteworthy. Had the action of the nicotinic acid been purely depression then the revival of the heart would have been a much more difficult task, while here the recovery was so quick.

The obvious explanation seems to be that Ringer's solution diluted the drug and this diluted drug had a stimulant action on the heart as is demonstrated by the powerful beats that followed. The circus movements of the ventricle, the increased amplitude and the tone, all these factors go to point out strong contractions of the ventricular musculature. This shows very well that nicotinic acid has a powerful action on the heart.

The results shown in figure 1 (plate XVII) were not obtainable with further dilutions. From the dilution 10^{-5} onwards the depression phase was absent. There was only stimulation of the heart beat followed by depression. In figure 2 (plate XVII) are given the tracings of a typical action with a diluted solution. The heart was being perfused with Ringer's solution R/10 and then a diluted solution of nicotinic acid, one part in ten millions of Ringer's solution, was perfused. At once there was a ready initial stimulation and then a gradual fall. The experiment on a fresh heart was started at 11.28 a.m. and the observation was made at 2.28 p.m. Since 3 hours had already elapsed when this particular dilution was started there was yet another proof of the proposition that nicotinic acid prolongs the life of the heart when it is perfused with that solution. Ordinarily, the heart ought to have stopped much earlier, *viz.* within half an hour (Burridge, 1935), while in the experiment in question the heart went on beating for $7\frac{1}{4}$ hours.

It is apparent from figure 3 (plate XVII), which should be considered along with figure 2 (plate XVII), that the heart was beating better at the end of $7\frac{1}{4}$ hours than what it

was after 3 hours judging from the amplitude, although the beats were not so regular. There are a few ventricular beats too weak to pull the lever down and hence the impressions appear irregular. The heart was showing some irregularity yet it was carrying on unabated.

Another similar experiment was done with a still more diluted solution, *viz.*, one part of nicotinic acid in 100 millions of Ringer's solution. In that case again the heart went on working and was still active at the end of 7½ hours when the laboratory was closed.

Concluding remarks.—The very first impression that one gets from the experiments detailed above is the behaviour of this drug in prolonging the activity of the heart. Normally the heart, if devoid of calcium as is the case in an unbalanced Ringer's solution, will stop after half an hour. If any drug can make the heart work in spite of calcium deficiency such a drug might be said to have the properties of 'calcium sparer'. But a closer examination shows that it is not a simple substitution process. In other words it is not that nicotinic acid can be substituted for calcium and vice versa. A Ringer's solution with its full quota of calcium will maintain activity longer than half an hour but not to the extent shown in my experiments. Besides, the amplitude in that case will fall constantly. But in the case of nicotinic acid the activity of the heart is what is called hysterical type and which according to Burrige (1935) is mediated by colloidal aggregation change.

We can, therefore, safely infer that the nicotinic acid enters into the composition of heart muscle and firmly binds its calcium.

Another feature worthy of note is the behaviour of the concentrated solution of nicotinic acid in arresting the heart in diastole. Unna (1939) found that a dose of nicotinic acid of 4 to 5 grammes per kg. body weight produced acutely toxic effects in mice and rats. Further, he found that a dose of 3 grammes per kg. body weight did not produce any toxic effects. Again he observed that nicotinic acid amide was more harmful. Luckily for us the average clinical dose of nicotinic acid is much too low to reach the toxic limit. Besides clinically the nicotinic acid is usually used when some deficiency of nicotinic acid is suspected. No doubt it is largely used empirically these days. But in these ailments the dose is even smaller than what it is in pellagra. With the advent of nicotinic acid amide people have started using it in so-called massive doses. Even these massive doses fail to get that concentration in the blood where toxic symptoms will supervene.

I submit that Unna's observation can be applied to human beings also. A trial of nicotinic acid on normal persons will lead to valuable conclusions as regards the toxicity. It is not right to believe that with the advent of nicotinic acid amide all the drawbacks of nicotinic acid have been conquered. It is worth

while to be fully conscious of its adverse effects on heart.

Nicotinic acid has a direct effect on the heart musculature, a tonic influence as was apparent from the powerful beats and squirting after the temporary arrest with strong solutions. The dilated and irritable hearts of pellagrins lack this tonic effect.

Summary

1. Nicotinic acid exerts two main actions on the heart of a frog, one of depression and the other of stimulation.
2. Large doses of nicotinic acid exert both actions, small doses only cause stimulation.
3. Nicotinic acid enters into firm chemical union with the heart muscle of the frog.
4. Nicotinic acid is a powerful drug and is active in dilution of one part in thousand millions.
5. Findings regarding its possible toxicity to human beings are discussed.

I am deeply indebted to Professor W. Burrige for valuable suggestions throughout this work.

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SEROLOGICAL REACTIONS IN 'TROPICAL EOSINOPHILIA'

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As part of the research into the ætiology of the disease syndrome now popularly called 'tropical eosinophilia' (Weingarten, 1943), an investigation into the serological changes if any as demonstrated by the Weil-Felix (OX19 and OXK), Wassermann and Kahn tests was undertaken during the past nine months. This condition has also been variously specified as 'pseudotuberculosis' (Frimodt-Møller and Barton, 1940), 'eosinophil lung' (Chaudhuri, 1943) and 'pulmonary acariasis' (Soysa and Jayawardena, 1945); and would also appear to be identical with 'lecithinophile eosinophilia' (Greval, 1940).

Weil-Felix agglutination with Proteus OX19 and Proteus OXK.—Carter, Wedd and D'Abbrera (1944) and Carter and D'Abbrera (1946), whilst recording the presence of forage mites in the sputum of patients suffering from

'tropical eosinophilia', advanced the view that this disease 'may in part at least be explained on the basis of mite infestation of the respiratory system'. As rickettsial-bodies are frequently found in the alimentary tracts of mites and as they are also the causative organisms of certain mite-borne diseases, the possibility of a hitherto unknown mite-borne rickettsia being responsible for this syndrome was considered. The agglutination tests with *Proteus* OX antigens being the ones available for the diagnosis of the known rickettsial diseases, the blood sera of six patients were tested for agglutination with type OX19 and type OXK. All six were negative. Of these six cases the sputum of five cases nos. 1, 2, 3, 7 and 15 was positive to mites whilst the sputum of the sixth case, no. 8, was not examined (*vide* table I).

Wassermann and Kahn tests.—Twenty-seven patients were investigated but only two cases, nos. 1 and 24, gave a history of syphilis and that too was contracted over ten years ago. Both patients soon after the manifestation of suspicious clinical symptoms had received a course of N.A.B. injections although their Wassermann reactions had been negative. These two cases though included in table I are not taken into account for statistical purpose (*vide* table II).

3, 7, 10, 15, 18 and 27 were positive, the number of samples of sputum examined from each patient being restricted to three 24-hour specimens only.

The Wassermann reaction was carried out according to the method of Wyler (1929) using 1 in 30 human heart antigen. With the serum of case no. 26 the test was repeated using ox heart antigen, the results obtained with both antigens being identical.

The standard Kahn test using ox heart antigen was the method used for obtaining the Kahn reaction. With the serum of case no. 26 the test was also performed with human heart antigen, the same degree of flocculation being obtained as with ox heart antigen.

All the cases, except case no. 27 which will form the subject of a further paper, were treated with leucarsone (M.&B.), the positive reactions becoming negative after the second course of treatment.

Significance of results.—In the series, out of nineteen cases (76 per cent) whose serum gave positive Wassermann reaction, only two gave a ++ Kahn and both these were children whose parents were untainted. The combination of a ++ Wassermann together with a ++++ or +++ Kahn, which is considered pathognomonic of syphilitic sera, was absent from the whole series, but what appeared to be a very

TABLE I
Summary of case records

Case number	Age	Sex	Occupation	Clinical phase*	W.B.C.	Absolute eosinophils	Eosinophils, per cent	Wassermann†	Kahn‡
1	64	M.	Pensioner	A	23,200	11,230	48.4	0	0
2	13	M.	Student	A	28,600	17,790	62.2	++	++
3	21	M.	Bank shroff	A	23,800	13,450	56.5	++	++
4	59	M.	Tailor	A	23,600	13,900	58.9	0	0
5	32	M.	Analyst	B	9,600	3,015	31.4	±	±
6	22	F.	B	25,400	13,590	53.5	++	++
7	37	M.	Radio inspector ..	A	10,000	1,360	13.6	+	0
8	32	M.	Assistant at printing office	B	16,500	8,380	50.8	++	0
9	41	F.	B	20,000	8,840	44.2	++	++
10	28	M.	Assistant at printing office	B	20,200	14,060	69.6	++	++
11	33	M.	Clerk	A	32,000	22,080	69.0	++	++
12	8	F.	Student	B	25,000	11,350	45.4	++	++
13	32	M.	Music teacher	A	26,000	16,510	63.5	±	0
14	30	M.	Customs clerk	A	8,600	4,770	55.5	++	±
15	50	M.	Clerk	B	27,000	17,010	63.0	±	±
16	51	M.	Merchant	B	17,000	8,750	51.5	0	0
17	46	F.	A	16,000	5,810	36.3	0	0
18	47	M.	Lorry driver	A	35,000	25,450	72.7	0	0
19	12	F.	Student	A	14,000	2,790	19.9	++	0
20	50	F.	A	33,200	26,590	80.1	++	++
21	40	F.	Clerk	A	16,200	10,000	61.7	+	±
22	32	F.	A	28,400	22,610	79.6	++	++
23	23	M.	Engineering apprentice	A	18,000	11,320	62.9	++	±
24	38	M.	A	12,400	6,520	52.6	++	++
25	29	M.	Teacher	B	17,000	6,290	37.0	++	±
26	26	M.	Assistant at printing office	A	15,600	10,860	69.6	++	++
27	34	M.	Clerk	A	18,200	9,660	53.1	++	++

* A = Asthmatic phase. † Wassermann = ++, +, ±, 0.

B = Bronchitic phase. ‡ Kahn = ++++, +++, ++, +, ±, 0.

The sputum of twelve patients only was examined for mites, *viz.* nos. 1, 2, 3, 4, 7, 9, 10, 11, 13, 15, 18 and 27. Of these, eight, *viz.* nos. 1, 2,

characteristic combination for this syndrome, a condition reported by Menon (1945), was a positive Wassermann with a doubtful or negative

Kahn (+ or ± being considered doubtful) (*vide* table II). Seventeen patients (68 per cent) gave this combination as against four (57 per cent) out of seven as recorded by Menon.

TABLE II
Combinations of Wassermann and Kahn

Wassermann	Kahn	Number of cases	Percentage
++	++++ or +++	Nil	
++	++	2	8
++	+	14	56
	or ± or 0		
+	+	3	
	or ± or 0		
± or 0	+	6	24
	or ± or 0		

Greval *et al.* (1938) considered that the corrected positive rate for an unselected Indian population should be under 10.25 per cent*, the crude rate obtained by them being 12.75 per cent. Katugampola (1944) found that out of 169 sera from Ceylonese cases where evidence of syphilis alone was excluded there were 4 per cent positives with Kahn and 11 per cent positives with the Wassermann using 1 in 30 antigen. The probable positive Wassermann rate for Ceylon was therefore found to be 11 per cent. With syphilitic sera, however, he found that 1 in 30 antigen gave 92 per cent positive Wassermann reaction in untreated cases, whilst the same sera gave 93 per cent positive Kahn.

Evidence that a high percentage of positive Wassermann is obtained in 'tropical eosinophilia' is now accumulating, but whether it is correct terminology to designate such a reaction in a non-syphilitic as a 'false positive' is we consider questionable.† The Wassermann test was introduced as an aid to the diagnosis of syphilis but positive reactions have been found in non-syphilitics suffering from leprosy, malaria, kala-azar, tuberculosis and now 'tropical eosinophilia'. It would therefore scarcely seem scientific to call the same visual manifestation denoting an inhibition of lysis a 'positive reaction' when investigating syphilis and a 'false positive reaction' when the disease is not syphilis.†

The mechanism which produces the positive Wassermann is not quite understood. Greval

considers that certain tropical diseases which give a positive Wassermann do so owing to the affinity of a substance in the blood serum for the lecithin in the W.R.-antigen. If this is so it means that two bacterial and two protozoal agents could produce this substance in the blood serum of their hosts. The nature of this substance can only be surmised, being either a true antibody or a reagin. If it is a true antibody it only means that *Mycobacterium lepræ*, *Mycobacterium tuberculosis*, the plasmodia of malaria, *Leishmania donovani* and the causative agent of 'tropical eosinophilia' contain a common antigenic component which is also present in *Treponema pallidum*. On the other hand if it is a reagin as suggested by Kolmer and Tuft (1941) the atopens or allergens which go into the composition of these various dissimilar ætiological agents also can provoke its production during the course of the disease.

Acknowledgments.—We have to thank Messrs. D. C. Katugampola and J. C. F. de Silva, laboratory assistants of the Institute of Bacteriology, for performing the serological reactions and to Mr. P. G. Jeyaratnam, laboratory assistant of the Division of Medical Entomology, for help in the preparation and examination of specimens of sputum for mites.

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SOME EXPERIMENTS ON TOQUE MONKEYS WITH TYROGLYPHID MITES

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THIS note records the results of three experiments carried out on two young adult male

* A later estimate by Greval and Sen is 'under 5.3 per cent' (*Indian Med. Gaz.*, LXXVII, 1942, p. 211).—EDITOR, *I.M.G.*

† 'False positive' is a convenient term. Otherwise a long explanation must be added to record the fact that although giving the usual reaction of syphilis the case is free from syphilis clinically.—EDITOR, *I.M.G.*

Toque monkeys (*Macaca sinica sinica* Linn.) with a species of mite which has been provisionally identified as *Tyrophagus putrescentiae* Schr. (*Tyroglyphus longior* Gerv.). The mites used in the experiments were bred in the laboratory from an original pair collected from infested onions. Morphologically, these mites appeared to be indistinguishable from one of the species recorded from, and commonly found in, the sputum of persons suffering from certain respiratory disorders in Ceylon, notably spasmodic bronchitis and asthma associated with high eosinophilia (see Carter, Wedd and D'Abbrera, 1944; Soysa and Jayawardena, 1945; Carter and D'Abbrera, 1946).

Methods employed in rearing mites and preparing mite extracts.—Mites from the original pair were reared in 15 c.mm. plate-cemented cavity slides containing particles of 'kraft' cheese and wheat germ as food. These slides were closed with cover-slips and kept in glass desiccators, the lower compartments of which contained a little water. When eggs were required for experimental purposes (see experiment no. 1) they were lifted from the slides with a fine paint brush under a low-power binocular microscope and transferred, immediately prior to use, to a glass block containing $\frac{1}{2}$ c.cm. of distilled water. Rearing mites in bulk for the purpose of preparing the mite extract was done in small petri dishes containing wheat flour and wheat germ; these were also kept in desiccators. When a plentiful supply of the mites was available, distilled water was run into one of the petri dishes and the contents well stirred; an equal quantity of anæsthetic ether was then added and the contents again stirred. The ether and the dead mites separated on the surface and were drawn off and transferred to a glass suction mortar; transference of the mites to the mortar was done gradually under the microscope until 1,000 mites had been counted. When the ether had evaporated the mites were thoroughly ground for about one hour in distilled water, measured quantities of which were added as required; when disintegration appeared to be complete a further quantity of distilled water sufficient to bring the total amount to 15 c.cm. was introduced. The extract so prepared was then transferred to a sterile test-tube and placed in a refrigerator; that used in experiments nos. 2 and 3 had been in cold storage for three months, and on being cultured was found free from bacterial contamination. The turbidity of the extract used was comparable with that of tube no. 3 of the Wellcome opacity tubes.

Experiment no. 1.—Monkey 'M' (table I). Attempted infestation of the respiratory tract with mites.

On 16th February, 1944, approximately 200 eggs of *T. putrescentiae* were introduced, via the mouth, by means of a specially constructed pipette into the trachea of monkey 'M' (body weight 2.8 kilogs.) which had previously been

anæsthetized with chloroform. To test the viability of these eggs, 20 from the same batch were placed in a clean cavity slide, provided with food and kept in the desiccator; all hatched on 17th February, 1944, and on 29th February, 1944, the mites had reached the adult stage and some were pairing; oviposition commenced on 3rd March, 1944.

Immediately prior to the introduction of the mite eggs into the trachea an examination of the blood of this monkey gave a total leucocyte count of 10,000 per c.mm. and an eosinophil count of 600 per c.mm. After the operation the monkey was returned to its cage where on the following day it developed slight pyrexia and cough which, however, quickly disappeared. During the ensuing six or seven weeks it was in good health and condition, but from April to the end of June suffered from an irregular and spasmodic cough with paroxysms occurring at intervals of a few days. Towards the end of March and in early April 1944, blood examinations showed increased leucocytes (16,000 and 14,600 per c.mm.), with a rise in eosinophils to 1,460 per c.mm. in April; but subsequently both counts decreased. From the end of May 1944 until August 1944, however, the blood showed increased eosinophilia ranging from 1,340 to 2,670 per c.mm. and from 9 per cent to 24.0 per cent of the total leucocytes; the latter during the same period varied from 9,600 to 15,000 per c.mm. From July 1944 onwards the monkey appeared to be in good health and no cough was observed. No sputum was obtainable for examination, but since it was thought probable that sputum was being swallowed, stomach washings were examined for mites on three occasions. No mites were found. Examinations of the faeces showed a few worm ova on one occasion, but none subsequently.

Experiment no. 2.—Monkey 'C' (table II). Injections of mite extract.

Subcutaneous injections of the Tyroglyphid extract were given to this monkey (body weight 2.5 kilogs.) as follows: 0.25 c.cm. on 13th May, 1944, 0.5 c.cm. on 14th May, 1944, and 1.25 c.cm. on 15th May, 1944.

Originally (on 16th February, 1944), an examination of the blood of this monkey showed total leucocytes 9,700 per c.mm. and eosinophils 870 per c.mm., but an examination made immediately prior to the first injection on 13th May, 1944, gave counts of total leucocytes 14,000 per c.mm. with eosinophils 420 per c.mm. On 15th May, 1944, prior to the last injection the counts were total leucocytes 12,500 per c.mm. and eosinophils 120 per c.mm. On 19th May, 1944, the eosinophils had increased considerably to 1,165 per c.mm. but three days later had dropped to 400 per c.mm. Two counts made during the ensuing fortnight showed total leucocytes 9,000 and 8,800 per c.mm. and eosinophils 540 and 620 per c.mm. The monkey was in good health and condition throughout the period involved.

TABLE I
Blood findings—monkey 'M'*
(Numbers per c.mm.)

Date of examination	Total leucocyte count	Neutrophils	Lymphocytes	EOSINOPHILS		REMARKS
				Number	Per cent	
<i>Experiment 1</i>						
16-2-44	10,000	3,500	5,600	600	6.0	16-2-44—200 eggs of <i>Tyrophagus</i> introduced into trachea.
23-2-44	9,250	1,050	7,300	550	5.9	
3-3-44	11,800	6,500	4,370	590	5.0	
14-3-44	11,000	2,650	7,600	660	6.0	
24-3-44	16,000	7,200	7,850	640	4.0	Irregular and spasmodic cough, April to June 1945.
6-4-44	14,600	2,480	10,220	1,460	10.0	
22-2-44	11,200	1,700	8,600	670	6.0	
13-5-44	9,800	3,800	4,900	690	7.0	
26-5-44	13,400	6,570	5,230	1,340	10.0	
4-6-44	11,000	2,530	5,720	2,640	24.0	
15-6-44	11,500	2,530	6,440	2,180	18.9	
25-6-44	11,600	2,440	6,270	2,670	22.9	
5-7-44	14,400	6,900	5,480	2,010	13.9	
26-7-44	9,600	870	7,000	1,630	17.0	
19-8-44	15,000	1,950	11,250	1,350	9.0	
<i>Experiment 3</i>						
2-1-45	19,200	4,700	12,370	2,130	11.1	Injection 0.5 c.c. mite extract. Injection 1.0 c.c. mite extract. Injection 1.5 c.c. mite extract. Injection 2.0 c.c. mite extract.
14-3-45	19,400	3,630	12,850	2,890	14.9	
16-3-45						
9-4-45	14,000	2,930	10,100	730	5.2	
18-4-45						
25-4-45	15,400	2,990	11,240	750	4.9	
2-5-45	18,400	4,820	12,770	390	2.1	
16-5-45	14,800	2,340	11,880	310	2.1	
23-5-45	14,200	2,400	11,020	440	3.1	
20-6-45	10,200	3,120	6,580	200	2.0	

TABLE II
Blood findings—monkey 'C'*
(Numbers per c.mm.)

Date of examination	Total leucocyte count	Neutrophils	Lymphocytes	EOSINOPHILS		REMARKS
				Number	Per cent	
<i>Experiment 2</i>						
16-2-44	9,700	2,330	6,020	870	9.0	Injection 0.25 c.c. mite extract. Injection 0.5 c.c. mite extract. Injection 1.25 c.c. mite extract.
13-5-44	14,000	2,100	11,480	420	3.0	
14-5-44						
15-5-44	12,500	5,130	7,120	120	1.0	
19-5-44	14,600	5,260	7,740	1,165	8.0	
22-5-44	10,000	2,000	7,300	400	4.0	
26-5-44	9,000	3,780	4,500	540	6.0	
4-6-44	8,800	1,050	6,780	620	7.0	
<i>Experiment 3</i>						
2-1-45	12,000	2,740	8,850	410	3.4	Injection 0.5 c.c. mite extract. Injection 1.0 c.c. mite extract. Injection 1.5 c.c. mite extract. Injection 2.0 c.c. mite extract.
14-3-45	11,600	1,670	9,580	160	1.4	
16-3-45						
9-4-45	11,000	1,270	9,140	250	2.3	
18-4-45						
25-4-45	11,200	1,420	9,400	260	2.3	
16-5-45	14,600	2,610	11,500	320	2.2	
23-5-45	15,400	2,970	11,780	370	2.4	
20-6-45	14,000	4,540	8,850	420	3.0	

* Bilimoria (1931) gives the mean differential count of 27 normal Indian monkeys (*Macaca sinica* and *M. rhesus*) as, neutrophils 35 per cent, lymphocytes 61 per cent, eosinophils 2 per cent, and large mononuclears 2 per cent, with a mean value for the total white cell count of 18,129.

Experiment no. 3.—Monkeys 'M' and 'C' (tables I and II). Injections of mite extract.

Mite extract was administered subcutaneously to both monkeys in increasing doses of 0.5 c.cm., 1 c.cm., 1.5 c.cm., and 2 c.cm. on 16th March, 1945, 9th April, 1945, 18th April, 1945, and 25th April, 1945, respectively. In the case of monkey 'M', 13 months had elapsed since the experimental introduction of mite eggs into the trachea and save for a sustained increase in eosinophilia the animal had for the last nine months been in good health with no cough or other bronchial symptoms. Monkey 'C' which had received an injection of mite extract 10 months previously was also in good health. The results of blood examinations of both monkeys made on 2nd January, 1945, and 14th March, 1945, are given in tables I and II, but it may be noted that whereas on 14th March, 1945, monkey 'M' showed an eosinophil count of 2,890 per c.mm. (14.9 per cent), monkey 'C' showed a count of only 160 per c.mm. (1.4 per cent). Three weeks after the first injection of mite extract the eosinophil count of monkey 'M' had dropped considerably 730 per c.mm. (or 5.2 per cent) and following the subsequent injections further reductions occurred. At the final examination made 8 weeks (on 20th June, 1945) after the last injection the eosinophil count was 200 per c.mm. The blood of monkey 'C' showed little change in respect of the eosinophils, the counts made subsequent to the injections of mite extract being somewhat higher than that made on 14th March, 1945, but lower than those observed on 2nd January, 1945, and in the previous experiment (no. 2).

Observations.—Although no positive evidence that the introduction of the eggs of Tyroglyphid mites into the trachea of monkey 'M' resulted in infestation—temporary or prolonged—of the respiratory system was obtained, the occurrence of bronchial symptoms some weeks after the operation and the sustained rise in the eosinophilia are, we suggest, matters of considerable interest in relation to the view that infestation by mites of the human respiratory tract may be an important factor in the aetiology of 'tropical eosinophilia' and associated conditions. The very definite reduction in eosinophilia in the same monkey following injections of the extract obtained from the same mites is also of interest, and may conceivably indicate a process of specific desensitization analogous to that reported by Figley (1929) and Harley (1942) who respectively and successfully used extracts of mayflies and pollen in the treatment of persons suffering from asthma and hay-fever. In these cases the effect of the desensitization upon the eosinophilia is not mentioned, but Greval (1940) using peptone obtained a non-specific desensitization with remission of asthma and reduction in eosinophilia (from 45 per cent. to 5 per cent) in one of his cases.

Summary

1. Three experiments on Toque monkeys with laboratory-bred Tyroglyphid mites—probably *Tyrophagus putrescentiae*—are described.

2. In the first experiment approximately 200 mite eggs were introduced into the trachea of a monkey. About seven weeks later the monkey developed an irregular and spasmodic cough which continued for three months, during which period the eosinophil count fluctuated but from about the sixth week onward showed a sustained increase. The increase in eosinophils remained after the cough had disappeared, and was still present eight to ten months later when further blood examinations were made in connection with a subsequent experiment.

3. In a second experiment on another monkey, 2 c.cm. of mite extract was administered subcutaneously over three days in three increasing doses. The injections of the extract were associated with a sharp but transient rise in eosinophilia; but no other effects were apparent.

4. In a third experiment, subcutaneous injections of mite extract aggregating 5 c.cm.—administered in four doses over a period of five weeks—were given to each of the monkeys involved in the previous experiments. No deleterious effects on the health of the animals were observed, but whereas the eosinophil count of the monkey which was the subject of the first experiment dropped rapidly from over 2,000 per c.mm. to 730 per c.mm. and subsequently to 300 or 400 per c.mm., the eosinophil count of the monkey subjected to the second experiment showed no definite change. It is suggested that this reduction in the eosinophilia of the former monkey may indicate that a process of desensitization had taken place following administration of the mite extract.

We are indebted to Surgeon Lieutenant G. Wedd, R.N., for his collaboration during the early stages of these experiments, and to Professor O. Hill for his assistance and advice in performing the operation on the monkey in experiment no. 1.

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REGIONAL ENTERITIS (CROHN'S DISEASE)*

A CASE WITH MULTIPLE JEJUNAL STRICTURES

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IN 1932, Crohn, Ginzburg and Oppenheimer presented a series of 14 cases under the caption 'regional ileitis'. To quote their own words, 'We propose to describe in its pathological and clinical details, a disease of the terminal ileum, affecting mainly young adults, characterized by a subacute or chronic necrotizing, and cicatrizing inflammation. The ulceration of the mucosa is accompanied by a disproportionate connective tissue reaction of the remaining coats of the intestine, associated with formation of multiple fistulæ'. They had no specimen to illustrate the early phase of the disease; all their material consisted of resected bowels from chronic cases of one or two years' duration. In these, only the terminal ileum was involved. The lesions were of different ages, and consisted of oval mucosal ulcers on the mesenteric border (earliest changes), and thickening of the walls due to cedema and inflammatory exudate in the submucosa and the muscularis; later, there was a fibrostenotic process both in the bowel and its mesentery, and the mucosa became extremely atrophic. Histologically, various degrees of acute, subacute or chronic inflammation with variation in the predominance of polymorphs, round cells, plasma cells, and fibroblasts were encountered; giant cells were also striking in some of the sections, but tuberculosis was ruled out by further histological and bacteriological studies.

Harris, Bell and Brunn (1933) enlarged the concept of Crohn by describing the same lesion in the jejunum in two of their cases. They coined a new term 'chronic cicatrizing enteritis'. Meyer and Rosi (1936) described another case in which the jejunum was affected. Erb and Farmer (1935) reported an interesting study of peculiar cases of 'ileocolitis' in children masquerading as acute appendicitis. In one of their cases, with a post-mortem record, they found the ileum and the colon markedly cedematous and congested. The mucosa showed ulcerations confined to Peyer's patches and solitary lymphoid follicles. Histologically, the involved portions showed the ulcerations to be covered over with necrotic debris containing Gram-negative bacilli, while the submucosa showed extreme cedema with infiltration by mononuclears and a few polymorphs in the vicinity of the ulcer. The mesenteric glands showed various degrees of congestion, cedema and mononuclear accumulations in the sinuses. They observed, 'that the disease is closely

related to that variously described as "regional ileitis", "chronic cicatrizing enteritis" or "benign granuloma of the intestine", we have great reasons to believe'. The authors believed that their cases represented the early picture of the entity described by Crohn, and they further asserted, that in some cases at least, the cæcum and the colon were involved in addition to the ileum. Later, Crohn and Rosenak (1936) enlarged their original concept; in a new series of 60 cases of 'regional ileitis' they found 9 complicated by an associated colitis; they also mentioned that Colp *et al.* (Crohn and Rosenak, 1936) and Brown (Crohn and Rosenak, 1936) had recorded such cases. In their opinion 'the process is an involvement of both small and large intestine in a similar non-specific inflammatory process, the ileum reacting to the noxa as a granuloma, the large intestine as an ulcerative hyperplastic colitis. The relationship is usually sequential, not synchronous'. Though both the ascending and the transverse colon may be affected in a segmental fashion, the ileitis is the dominating feature of the disease, removal of the ileum curing the patient. Koster, Kasman and Sheinfeld (1936), reviewing 17 cases of their own, observed that the disease process could appear in any portion of the bowel, the location in the terminal ileum being more frequent than elsewhere.

The most important contribution to the study of pathology of the condition is that of Hadfield (1939). His observations in 20 cases of regional ileitis are very stimulating. Ulceration of various degrees was present in all cases but the most important lesions were in the submucosa and these preceded the ulceration. Here there was a widespread hyperplasia of the lymphoid tissue and an obstructive lymphœdema; but the characteristic histological features were proliferation of the endothelial cells in the germinal centres of the lymphoid tissue and formation of Langhans' type of giant cells from these cells. But these giant cell systems differed from those of tuberculous inflammation; there was no necrosis or destruction of the surrounding tissue, no caseation and acid-fast bacilli were found. In fact, after a time, the lesion retrogressed with definite increase in the reticulum but no gross fibrosis. In the regional lymph glands there were seen identical giant cell systems and the same march of events. With ulcerations and superadded infection these finer details were obscured by diffuse inflammatory exudate and widespread fibrosis. Hadfield suggested that the characteristic lesion of regional ileitis resembled very much that of Boeck's sarcoidosis. Commenting on this paper an annotation (Editorial, 1939) pointed out that the lesions described by Hadfield closely resembled the lesions produced in animals by inoculation of dead tubercle bacilli and the suggestion was made that regional ileitis may owe its features to the passage of dead bacilli, or their products, from the intestinal tract

* Read at the 52nd meeting of the teaching pathologists, Bombay.

into the submucosa and lymphadenoid tissue. Reichert and Mathes (Editorial, 1943) attempted to reproduce the condition experimentally. They injected irritating and sclerosing solutions into the mesentery. The obstructive lymphangitis thus produced, resulted in 'an elephantoid condition of the bowel simulating the early stages of regional enteritis'.

In this country, Manohar (1941) from the post-mortem material of our department has described a series of 51 cases of 'non-specific ulcers of the alimentary tract'; in 4 of these the jejunum was involved in a chronic process. It is possible that some of these cases might have been early cases of regional enteritis. Kini (1941), in a series of 30 cases of intestinal obstruction, came across 3 cases of 'annular stricture due to granulomatous ulcers'; the ileum was involved in all the three. Arawattigi (1943) feels that regional enteritis is fairly common in India; he came across 26 cases of 'granulomatous intestinal lesions without tuberculosis' in the course of four years. An interesting finding, in his series, is the recovery of *E. histolytica* from the faeces of a large number of the cases. Kaikini (1944), from this institution, has reported a case of 'regional ileitis'. None of these authors, however, came across involvement of the jejunum with stricture formation.

Case notes

A Hindu male, aged 40 years, was admitted with the complaint of pain in the abdomen. On questioning it was elicited that the pain was there off and on for three years, but worse for the last ten months. It was located to the upper part of the abdomen, was of a dull colicky type, continuous throughout the twenty-four hours, but worse after food. There was also a good deal of distension of the upper abdomen coming on half an hour after meals, followed shortly by vomiting. The vomiting was not projectile, and, relieved to a considerable extent, both the distension and the pain. There was no history of hæmatemesis. The patient was habitually constipated and passed blood per rectum off and on. There was no loss of appetite.

He used to take a mixed diet, smoked very moderately and had not touched alcohol for the last ten years, though habituated to taking it off and on before that. There was no history of any important previous illnesses.

On examination the patient was pale and emaciated. Temperature 98°F.; pulse 74; respirations 22 per minute. The abdomen was distended especially in its upper portion, but moved freely all over. There was no visible peristalsis. No rigidity was appreciated anywhere but the epigastrium over a wide area was definitely tender. No lump could be felt. Rectal and sigmoidoscopic examinations were negative. Other systems were normal.

In the laboratory investigations undertaken, the only abnormality noted was a positive occult blood test in the faeces.

X-ray examination, after a barium meal, showed no lesion in the stomach. There was marked dilatation of the duodenal canal and the proximal part of the jejunum. Obstruction was present in the jejunum distally. The x-ray diagnosis was 'jejunal stricture'.

After five days' observation in the wards the patient was operated upon. The notes taken down at the operation were as follows: 'The peritoneal cavity did not show any free fluid. In the region of the appendix conspicuous adhesions were noted. On tracing the small bowel, in the length of the jejunum, were seen four strictures within a length of a foot and a quarter. The affected portions of the bowel and its mesentery were excised and a gastrojejunostomy was done. Other organs in the abdominal cavity appeared normal. The mesenteric lymph glands were not enlarged'. A blood transfusion and intravenous saline were given during the operation. The post-operative period was very stormy; there was a rise of temperature, vomiting, and distension of the abdomen. Another transfusion was given but the patient died on the 7th day of the operation. Permission for a post-mortem examination was refused.

The specimen (see figures 1 and 2, plate XVII) was that of the small intestine and measured 37 cm. in length. The bowel was extremely constricted at four places, and ballooned out in between. The peritoneal surface appeared quite normal, except at the site of one of the constrictions; here was seen congestion over an area embracing one-third the circumference of the bowel. The attached mesentery was normal, but at the sites of the constrictions could be felt to be thickened; no lymph nodes could be seen, or felt in the portion of the mesentery resected. On opening the bowel, the existence of the strictures was confirmed; the narrowing was severe enough to reduce the lumen to less than one-sixth the normal. The folds of the mucosa were well preserved, and there was no hypertrophy or thinning of the bowel wall. At the site of the strictures, however, the mucosal folds were lost over a width of 2 to 4 cm. along the whole circumference of the intestine. Here the mucosa appeared denuded, but there were no sloughs and the edges of the bald areas were quite smooth. Here the wall of the bowel could be felt to be firm and unyielding. A careful examination, with the aid of a magnifying lens, did not show any tuberculous nodules in any portion of the resected bowel.

Histological examination

One of the strictures was sacrificed for histological study. Four blocks were prepared and the sections were stained with: (1) Hæmatoxylin and eosin, (2) Reticulum stain (Foot), (3) Ziehl-Neelsen stain for acid-fast bacilli. The histol-

ogical details were as follows: The mucosa showed loss of the surface epithelium at many places; at some spots even the glands had almost disappeared. In the lamina propria lymphocytes and eosinophils were present in normal numbers but the plasma cells were greatly increased and there was some fibroblastic proliferation as well. In some of the sections, newly formed capillaries running perpendicular to the surface were quite prominent. Not much necrotic debris was seen on the surface and organisms could not be made out. In the region of deeper ulcerations the muscularis mucosæ could not be traced. The submucosa was markedly thickened. In it could be seen, in some of the sections, solitary lymphoid follicles with reactive germinal centres. There was much lymphœdema in this coat. The most conspicuous feature, however, was the intense infiltration by plasma cells, mostly diffuse, but at spots of deep ulcerations, collected into dense aggregates. Lymphocytes and mononuclears were present in moderate numbers, and an occasional eosinophil was also seen. Careful search showed a solitary giant cell of Langhans' type. The muscular coat did not show any appreciable hypertrophy, but there was the same plasma cell infiltration in its interstices, though much less than in the submucosa. The serosa also showed accumulations of plasma cells here and there.

Sections through the substance of the stricture showed a complete destruction of the normal pattern of the intestine. The mucosa showed a few remnants of glands and the muscularis mucosæ could not be identified at all. The muscularis, wherever it could be traced, was much more infiltrated with plasma cells than in the previous sections. As the muscular coat was traced further, it became lost in a large mass of collagen tissue crowded with plasma cells, but also showing eosinophils in fair numbers and a few mononuclears and polymorphs. Reticulum stain showed increased reticulum in the submucosa. Sections stained for acid-fast bacilli did not show any organisms after a prolonged search.

The clinical history, the gross anatomy and the histopathology suggested a diagnosis of 'regional enteritis'.

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EFFECT OF BLOOD DONATION ON THE HÆMPOIETIC SYSTEM

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STUDIES on the effect of repeated blood donations on the hæmopoietic system of donors were first made by Giffin and Haines in 1923, and later by many other workers, of whom mention may be made of Jones, Widing and Nelson (1931), Martin and Myers (1934), Merklen, Israel and Apffel (1936), Brinck and Oettinger (1937), Cadham (1938), Fukuda and Tominaga (1938), Brewer (1939), Snapper, Liu, Chung and Yu (1939), and Fowler and Barer (1942). The investigators, however, were not unanimous in their opinion. Though satisfactory response of the hæmopoietic system and no deleterious effects on general health were reported by majority of the workers, the incidence of anæmia, leucopenia and ill health following donations of blood was reported by some. A brief review of the various findings is given below.

In the case of the male donors, satisfactory regenerative power of the hæmopoietic system after multiple donations of 400 to 750 c.cm. of blood was noted by Giffin and Haines, Jones, Widing and Nelson, Martin and Myers, Brewer, and Fowler and Barer, and after small frequent withdrawals of 65 to 140 c.cm. of blood by Cadham (1938). The drop in the hæmoglobin value was found to be 4 per cent after donation of 400 c.cm. of blood by Jones, Widing and Nelson, 5.2 per cent after donation of 500 c.cm. by Martin and Myers, and 2.3 gm. after donation of 550 c.cm. by Fowler and Barer. Reduction in the erythrocyte count was found to be 300,000 after donation of 400 c.cm. by Jones, Widing and Nelson, and 310,000 per c.cm. after donation of 500 c.cm. by Martin and Myers. The regenerative power of the hæmopoietic system was found to be very quick in the male donors by Jones, Widing and Nelson, and Martin and Myers, after donation of 400 to 500 c.cm. of blood. While Brewer stated that the hæmoglobin returned to the normal level within 2 months after donation of 400 to 750 c.cm. of blood, and Fowler and Barer found that after removal of 550 c.cm. of blood, the average time for the hæmoglobin to reach

the pre-donation level was 49.6 days. The last-named workers also found that hæmoglobin was regenerated at the rate of 0.049 gm. in the males and 0.040 gm. in the females per day, that the rate of hæmoglobin regeneration appeared to be constant and bore no relation to the number of donations. They also noted that the administration of iron helped to regenerate hæmoglobin after early donations, but had progressively less effect after subsequent donations.

Most of these workers found that the female donors were not so satisfactory as the male donors; that in the females anæmia developed more quickly, was found in a larger number of cases, and the return to normal was delayed.

Less encouraging results about the regenerative power of the hæmopoietic system were given by Merklen, Israel and Apffel (1936), Brinck and Oettinger (1937), Fukuda and Tominaga (1938), and Snapper, Liu, Chung and Yu (1939). Fukuda and Tominaga found that 10 to 12 fortnightly donations of 100 c.cm. of blood resulted in the decrease of hæmoglobin, red cells and specific gravity of blood. Frank anæmia generally hypochromic in type was noted by Merklen, Israel and Apffel in 25 per cent of the donors and by Snapper *et al.* in 44 per cent of the donors. The high incidence of anæmia noted by Snapper *et al.* in the Chinese donors is attributed to the very poor economic status of these donors and inadequate diet, the most important factor of inadequacy being the complete absence of animal protein from the diet. Snapper and his associates also noted that cessation of blood donation did not invariably produce improvement but treatment with large doses of iron did and promptly too. Significant changes in the white cell count only, without any associated anæmia, were noted by Brinck and Oettinger.

The safe interval between two successive donations is given by Brewer as 3 months for males and 4 months for females. Almost similar views are held by Martin and Myers.

Subjects of study

Status.—There were fourteen donors in the group. The group was composed of one doctor, eight medical students, three laboratory assistants and two clerks.

Sex.—There were two females in this group.

Age.—The ages varied between 21 and 42 but the ages of 11 people out of the total 14 were below 30.

Religion.—There were two Anglo-Indians (case nos. 5 and 11), one Indian Christian (case no. 4), one Jew (case no. 14), and the remaining ten were Bengali Hindus.

Body weight.—Varied from 44.1 kg. to 82.7 kg. with an average of 60.3 kg.

Blood picture.—Both hæmoglobin and red cell count were well above the normal range in all the donors. The hæmatocrit reading, the mean corpuscular value, the total and differential

white cell counts, the sedimentation rate, and the van den Bergh reaction were all within the normal ranges in all cases.

Amount of blood donation.—Varied from 100 c.cm. to 400 c.cm. with an average of 218 c.cm.

Interval between two successive donations.—Always over 4 months, sometimes over 6 months.

Number of donations.—Varied from 2 to 17.

Methods of investigation

Complete cytological examination of blood including hæmatocrit reading, erythrocyte sedimentation rate, and van den Bergh test was done in all the donors before the donation of blood. Post-donation examination of blood was done daily or as often as the donors presented themselves for the examinations, and was continued wherever the donors collaborated, till the blood picture returned to the pre-donation level. Two of the donors (case nos. 2 and 7) were studied twice in course of two donations and the rest only once during a particular donation.

Effect of blood donation on blood picture (see table)

(i) **Effect on hæmoglobin.**—The fall in hæmoglobin was variable and varied from 0 to 1.7 gm. with an average of 0.8 gm. The maximum drop in hæmoglobin was 1.79 gm. noticed in donor no. 2(a) after donation of 400 c.cm. of blood in his 11th donation. A fall of 0.69 gm. of hæmoglobin was noted in the same donor after donation of 225 c.cm. of blood in his 15th donation. No fall in hæmoglobin was noted in case no. 11 after donation of 150 c.cm. of blood. The maximum drop in hæmoglobin was generally found within 48 hours; in two cases, however, it was noted on the 6th day and in another case on the 7th day. In most cases the hæmoglobin reached the pre-donation level in 2 to 4 days; in a few cases it took over 15 days for the hæmoglobin to reach the pre-donation level. Except in the case cited above [case no. 2(a)] there does not appear to be any correlation between the fall in hæmoglobin and the amount of blood donation or the number of donations. Nor there is a correlation between the recovery time and the amount of the blood donation or the number of blood donations.

(ii) **Effect on red cells.**—The drop in red cells was also variable and ranged from 0 to 2,070,000. There was no fall in the red cell count in 3 cases (case nos. 12, 11 and 5) after donation of 100, 120 and 300 c.cm. of blood, respectively. The maximum fall of 2,070,000 per c.cm. was again noted in donor no. 2(a) after donation of 400 c.cm. of blood in the 11th donation. The same donor was examined a second time in his 15th donation when he donated 225 c.cm. of blood; this time a fall of 0.330,000 in the red cell count was noted.

The maximum drop in the red cell count generally occurred within 3 days of donation; in two cases (case nos. 8 and 13) the maximum

A table giving blood pictures of 14 donors

Donor number	Weight in kg.	Age	Sex	Donation number	PRE-DONATION		Quantity donated in c.cm.	HEMOGLOBIN			RED BLOOD CELLS			CELL VOLUME		
					Hb.	R.B.C.		Maximum drop in gm.	When observed	Regeneration time in days	Maximum drop in million	When observed	Regeneration time in days	Maximum drop in per cent	When observed	Regeneration time in days
1	73.6	38	M.	17	18.15	6.05	250	1.52	1st day	* Between 15 and 21	0.4	3rd day	* Between 15 and 21	1.4	4th day	15
2(a)	52.7	29	M.	11	14.71	5.82	400	1.79	6th day	* Between 9 and 40	2.07	3rd day	* Between 9 and 40	4.4	2nd day	* Between 9 and 40
2(b)	53.6	30	M.	15	17.87	6.25	225	0.69	2nd day	4	0.33	2nd day	4	1.4	2nd day	19
3	63.6	41	M.	12	16.5	5.11	250	1.37	2nd day	4	0.55	3rd day	4	3.1	2nd day	11
4	50.0	42	M.	11	16.91	5.78	250	0.27	1st day	2	Nil	3.7	1st day	..
5	62.7	22	M.	4	16.36	5.10	300	0.28	1st day	2	Nil	1.4	1st day	3
6	82.7	23	M.	5	16.91	5.89	250	0.55	2nd day	4	0.05	1st day	4	5.0	1st day	† Over 7
7(a)	57.2	29	M.	2	16.64	5.28	200	0.14	1st day	2	0.04	1st day	2	2.0	2nd day	† Over 2
7(b)	57.2	29	M.	3	16.50	5.92	100	0.83	1st day	* Between 4 and 7	0.52	2nd day	* Between 4 and 7	5.1	2nd day	† Over 7
8	59.1	22	M.	2	15.40	5.20	200	1.1	7th day	* Between 15 and 23	0.40	6th day	* Between 15 and 23	2.2	2nd day	* Between 15 and 23
9	55.4	22	M.	2	15.26	5.1	150	0.55	1st day	3	0.19	2nd day	..	2.4	2nd day	3
10	53.66	21	M.	2	16.78	5.78	300	1.65	1st day	?	1.140	1st day	?	4.7	1st day	?
11	76.3	24	M.	2	15.95	5.04	150	Nil	Nil	Nil
12	61.8	30	M.	2	17.87	5.18	100	0.27	1st day	2	Nil	1.0	1st day	4
13	44.1	20	F.	4	13.75	5.18	150	0.83	6th day	* Between 14 and 24	0.60	6th day	* Between 14 and 24	2.0	3rd day	* Between 14 and 24
14	51.3	22	F.	2	15.4	4.78	250	0.65	5th day	?	0.44	5th day	?	1.8	5th day	?

In the cases marked with * and † the exact time taken for the blood value to reach the pre-donation levels could not be ascertained as the donors did not attend the clinic regularly.

* In these cases no blood examination was done in between the days mentioned in the table. The blood value had not reached the pre-donation levels on the first of the two days mentioned in the table but did so on the second day.

† No further examination of the blood could be done subsequent to the day shown in the table.

Had an attack of influenza on the 6th day.

Had an attack of influenza on the 4th day.

The donor did not attend after the 1st day.

The donor attended only once on the 5th day. Complained of great exhaustion after blood donation.

drop was noted on the 6th day. Generally, the red cell count reached the pre-donation level in 2 to 4 days; in one case it took more than 9 days and in three cases more than 14 days for the red cell count to reach the pre-donation level. If case no. 2(a) is excluded from the series, there does not appear to be any correlation between the fall in the red cell count or the recovery period and the amount and/or number of blood donations.

(iii) *Effect on reticulocytes*.—Reticulocytosis was not noted in any of the post-donation counts.

(iv) *Effect on white cell counts*.—No marked change in the total or differential white cell count was noted in any of the cases.

(v) *Effect on cell volume and mean corpuscular values*.—Except in one person, case no. 11, who did not show any change in the blood picture after donation of 150 c.cm. of blood, a fall in the hæmatocrit reading was noted in all other cases. In most cases the maximum fall was noted within two days after the blood donation and generally took more than 7 days for the cell volume to return to its pre-donation level. There does not seem to be any correlation between the fall in the cell volume and the fall in the red cell count; nor is there any correlation between the fall in the cell volume and the amount and/or the number of blood donations.

In spite of the changes in the red cell count, hæmoglobin value and cell volume, the mean corpuscular values were found to be always within the normal range.

(vi) *Indirect van den Bergh test*.—Plasma bilirubin was estimated quantitatively in all cases and found to be within normal range except in donor no. 2, during his 11th donation. In this case, the bilirubin content went up to 1.25 mgm. per cent on the 3rd day after donation. The hyperbilirubinæmia persisted till the 5th day and thereafter gradually returned to the normal level on the 9th day.

(vii) *Erythrocyte sedimentation rate*.—There was no variation in the sedimentation rate in any of the cases.

Other effects

A female donor, no. 14, complained of weakness and exhaustion after a donation of 250 c.cm. of blood; no such complaint was made by any other donor, not even by donor no. 2 in his 11th donation when his red cell count fell down by over 2 millions per c.cm. of blood.

Two donors, nos. 4 and 7(b), had attacks of influenza following blood donation; donor no. 4 on the 6th day and donor no. 7(b) on the 4th day after blood donation.

Discussion

All the donors in our series were suitable for blood donations both clinically and hæmatologically, so also were those of the American and European donors but not so those of the

Chinese donors. The dietary habit, excepting in the case of the two Anglo-Indian donors, was more akin to that of the Chinese donors and like theirs the diet was deficient in protein, especially of animal protein. The amount of blood donated was generally much smaller and the interval between two successive donations was much longer in the case of our donors, than in the cases of the American, European or even Chinese donors. Thus comparison between our results and those obtained by European, American and Chinese workers is not strictly justified. It will, however, be noted that even with the small amount of donation of blood, a fall in hæmoglobin, in red cell count and in cell volume, was noted in most of our donors, being quite appreciable in about 50 per cent of the cases. Excluding case no. 2(a), where the blood values fell considerably after donation of 400 c.cm. of blood, it will be seen that the fall in blood values was not influenced by the amount of blood donation, or by the number of donations, or by the pre-donation blood values. With very slight fall in the blood values, the blood picture returned to the pre-donation level within five days, but when the fall was appreciable it generally took 15 days or more for the blood picture to return to the pre-donation level. In case of the female donor, no. 13, whose blood was examined regularly, the blood values fell considerably after donation of 150 c.cm. of blood and the blood picture did not reach the pre-donation level even on the 14th day though she was a healthy girl with a red cell count of over 5 millions per c.cm.

An appreciable fall in blood counts with slow regeneration of blood was noted in some of the Bengali donors, in contrast to the very slight effect produced in the two Anglo-Indian donors and the Christian donor. Could this be attributed to the poor protein intake by the Bengali donors? It is well known that Bengali diet generally is rather unbalanced and poor in protein, specially protein from animal source. Anglo-Indians and Christians, on the other hand generally, have a more balanced diet with a fair amount of animal protein. The data, however, are too meagre to justify any definite conclusion.

Conclusion

From the available data, it may be concluded that the effect of blood donation on the hæmopoietic system in the donors varies from person to person and also varies in the same person at different periods; in other words, the effect of blood donation depends entirely on the hæmopoietic activity of the marrow of the individual at the moment. Also, other things remaining the same, the activity of the hæmopoietic system of an individual will probably be influenced by the protein intake of the individual.

To avoid any detrimental effect on the health of the donors after donation of blood, it is suggested that the donor should always be

examined not only clinically but also hæmatologically before each donation of blood; that the amount of blood to be donated by any donor should be judged from the weight, blood pressure and blood values of the donor; that generally not more than 300 c.cm. of blood should be taken out at one time from any Bengali donor; that the interval between two successive donations should never be less than 3 months in the case of male donors and 4 months in the case of female donors; and that the donor should be advised to take adequate animal protein, at least for 2 to 3 weeks after each donation of blood.

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POISONOUS FOODGRAIN: WHEAT MIXED WITH *LOLIUM TEMULENTUM*

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AN EPIDEMIC IN ADEN

In the March issue of this journal there appeared under 'Medical News' (p. 148; an abstract from an article by Brinton) an account of an epidemic at Aden caused by the seed of *Lolium temulentum*, a weed which grows in wheat fields. The wheat was brought from Abyssinia and milled locally by machinery. The consumption of the product made the inhabitants go down with symptoms of acute intoxication. For 13 months from October 1942 the population suffered intermittently. Some 450 persons suffered. From 1 hour to 2 hours after taking

food made from this grain a man became dizzy and developed headache, generalized tremors, lassitude, slurred speech and staggering gait. Nausea, abdominal pain, vomiting and diarrhoea were also in evidence at times. Those who had fed well became stuporous or even comatose for as long as 10 hours while those who had eaten only a little recovered in 3 to 4 hours. There were no deaths. All were well enough to resume their usual occupation in 72 hours.

The weed is said to be known to the farmers in Arabia as *Miscara* and is removed before the wheat is ready for reaping. This precaution was not taken in Abyssinia. The wheat mixed with the weed seed is sieved in Abyssinia and the seed removed before milling. This precaution was not taken in Aden. Ordinarily, in Asia, the housewife hand-winnows the wheat before milling and thus removes all grains other than wheat. This step was missed in Aden. Later, in the samples taken for examination, the weed seeds were found to be up to 10 per cent.

THE WEED

Historical.—The harmful nature of the grains of *L. temulentum* has been known for centuries and it possibly represents the 'tares' of the Scriptures. As early as 1789 it was stated that the seeds possess very intoxicating quality and bring on convulsions if taken in large quantities (Adam, quoted by Brenchley, 1920). The weed is known to Indian toxicologists (Owens, 1935; Modi, 1943). The plant is known in different countries by different popular and local names. The popular English name for it is 'darnel' or 'bearded wheat'. One of the many other local English names is the 'drunken plant' which proves the knowledge of the people about its effect on man (Brenchley, *loc. cit.*). The Arabian name *Miscara* which means tipsy describes its effect on man. In France darnel is called *Ivræ* and in Germany *Taumelloch*. In the Punjab and North-West Frontier Province of India the local names for it are *Mostaki* and *Mochni* respectively.

Distribution.—The plant is distributed throughout Europe and Northern Asia (Index Kewensis); in other places it has been introduced. It was reported from Argentina (Marchionatto, 1941) that the plant is a wild grass there and that the toxic nature of the seeds to man and animals is known to local people. In India it is found in the Upper Gangetic Plain, the Punjab, Sind and Western Himalayas, from 4 to 6,000 feet, and is an introduced plant in the Kashmir State (Hooker, 1897). It was introduced into Shillong, Assam, in the year 1934 (Bor, 1940). The plant is not reported from Bengal, Bihar, Orissa, Madras and Bombay (Prain, 1903; Haines, 1925, Gamble, 1928; Blatter and McCann, 1935). From the nature of distribution of the plant it appears that the darnel mixed with wheat grain, which produced the epidemic in Aden, was imported into Abyssinia from abroad.

* Not seen in original.

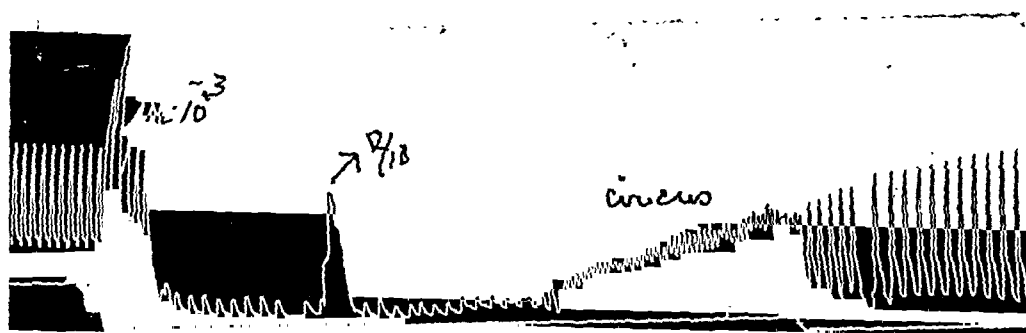


Fig. 1.—Composition of perfusing solution R/10, 0.6% NaCl, 0.03% KCl, 0.01% NaH CO₃, 0.0025% CaCl₂.
At—Ni 10⁻³ one part of nicotinic acid in one thousand of Ringer's solution R/10 perfused.
At—R/10 Ringer's solution alone began to be reperfused.
Circus—Circus movement of the ventricle.

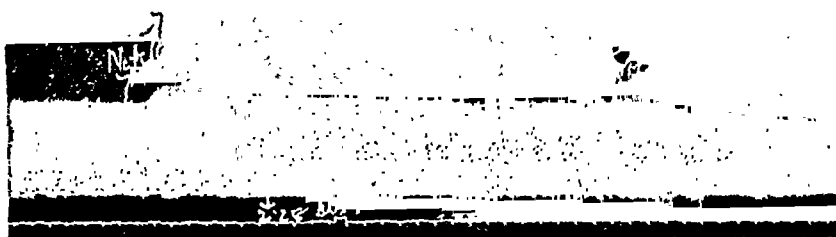


Fig. 2.—At—Ni Ac 10⁻⁷ nicotinic acid one part in 10,000,000 was perfused.
At—R/10 Ringer's solution reperfused.
At 2.28, 3 hours, duration of experiment.
Time in half minutes.

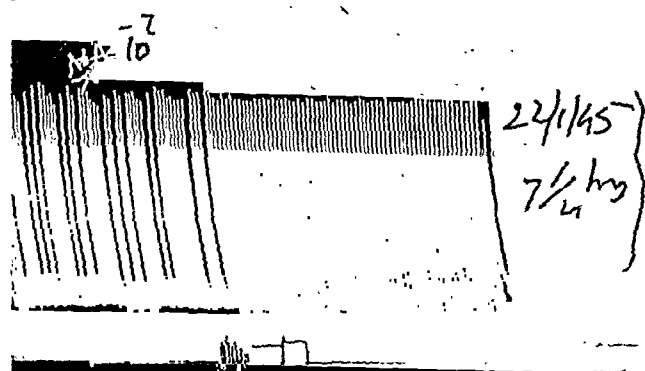


Fig. 3.—Notations as in figure 2.
22-1-45. Date of experiment.
7 1/2 hours. Duration of experiment.

REGIONAL ENTERITIS (CROHN'S DISEASE) : A CASE WITH MULTIPLE JEJUNAL STRICTURES : Y. M. BHENDE. PAGE 288.



Fig. 1.—Peritoneal surface : Shows three strictures and ballooning out of the intestine in between them.



Fig. 2.—The intestine opened up to show the mucosal surface.

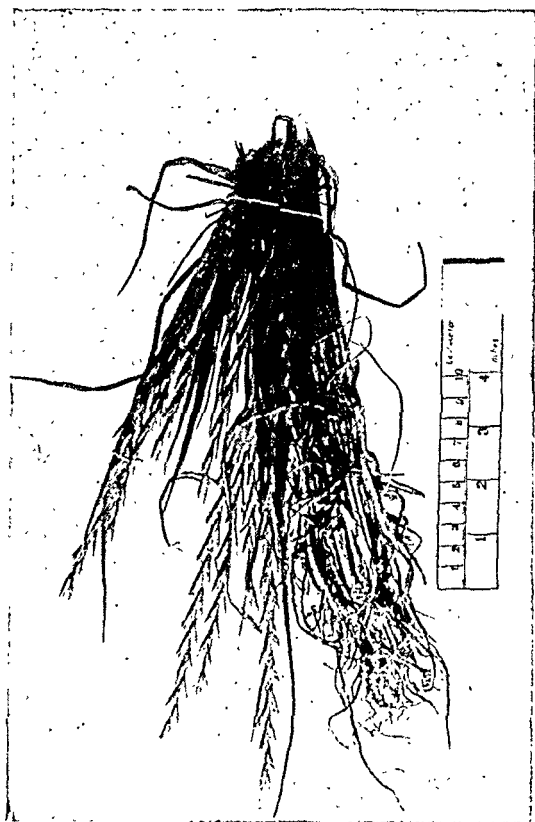


Fig. 1.—Showing *Lolium temulentum*. Many tillers together. Note lax spikelets in the ear.

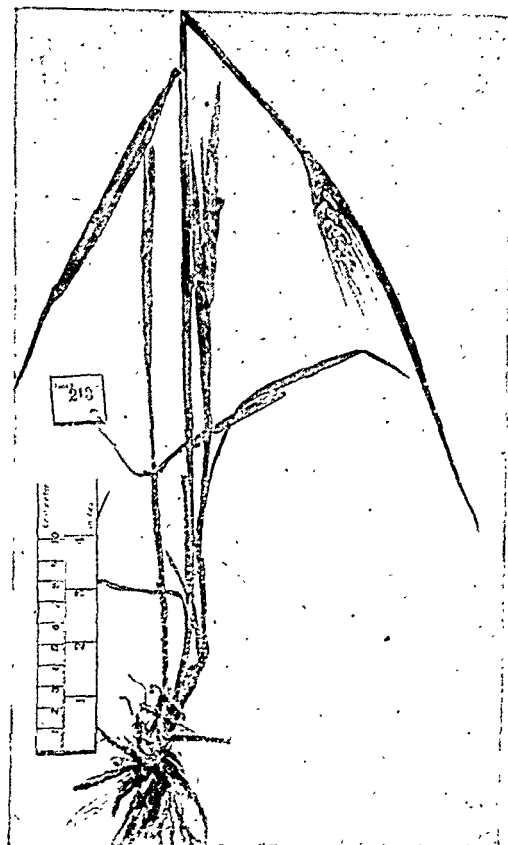


Fig. 2.—Showing *Triticum vulgare*. Only three tillers shown. Note compressed spikelets in the ear.

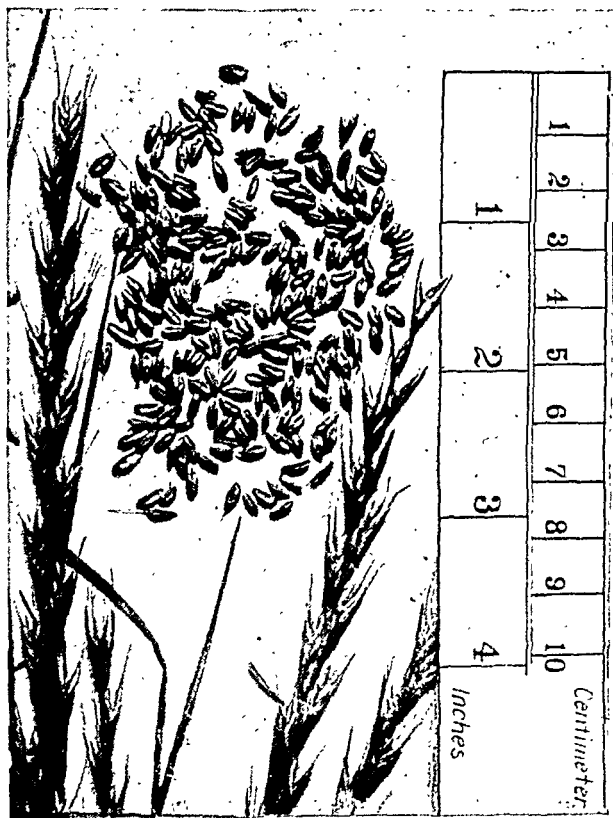


Fig. 3.—Showing grains of *L. temulentum*. Note a close resemblance to wheat in shape (not in size).

(For 'centimeter' read 'centimeters'.)

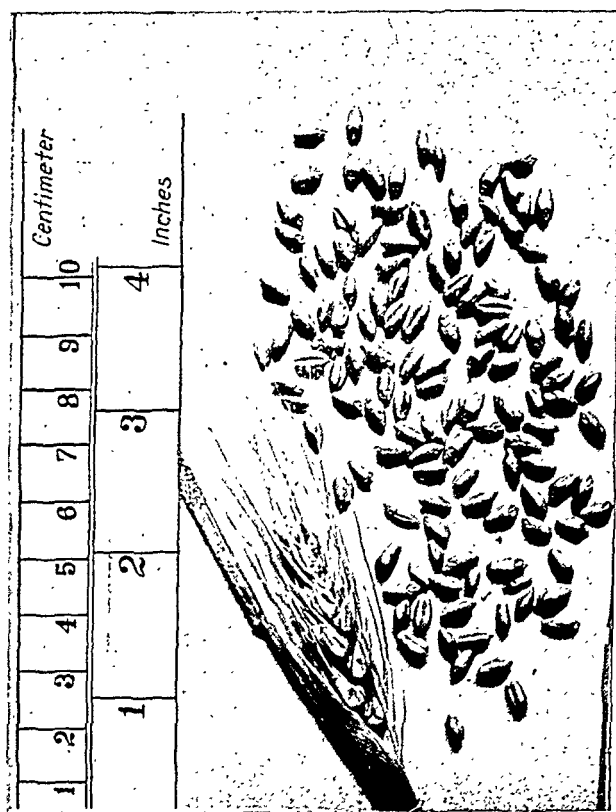


Fig. 4.—Showing wheat grains.

It is interesting to note that unlike *L. temulentum* other species of lolium are well known as fodder and pasture grasses, e.g. English rye-grass (*L. perenne*), Italian rye-grass (*L. multiflorum*) and annual rye-grass (*L. remotum*).

THE FUNGUS

It is now well established that the poisonous nature of *L. temulentum* grains is due to the harbouring of an endophytic fungus between the seed coat and the endosperm. The fungus lives symbiotically in the grains and is carried from one generation to the next through the germinating seedling to the developing ovary and finally to the mature grains. Grains of *L. temulentum* nearly always harbour the fungus and it is claimed that the harbouring plants are richer in nitrogen than the non-harbouring ones (Engler and Diels, 1936). Fresh lodgement occurs during spike formation (Marchionatto, 1941). On examination of seed samples in Argentina it was found that the fungus was present in 75 per cent of the grains of *L. temulentum*, 25 per cent of the grains of *L. multiflorum* and absent in the grains of *L. perenne*. The germinating capacity of non-harbouring seeds was however greater than that of the harbouring ones.

Attempts to isolate the darnel fungus were made in 1903 and 1906 (Freeman, 1903; 1906) and it was suggested that the fungus was related to the Ustilaginæ (smut fungi). Later, the endophytic fungus from wheat, barley and rye-grass (*L. perenne*) was isolated and said to be almost identical with the one present in *L. temulentum* (Jodidi and Peklo, 1929). After extensive observations it was concluded that these endophytic fungi are a special and new type of smut fungus, because they, unlike many other smuts which grow parasitically on wheat, barley and other cereals producing the 'Bunt disease', are typical symbionts. It has been shown also that the hyphæ contain 'prolamin', an alcohol soluble protein and an essential constituent of gluten, the latter being the characteristic protein of cereals and grasses and specially rich in the 'aleurone cells'.* This observation is specially interesting because on the one hand it supports the theory that the aleurone grains represent the products of the symbiotic fungi (Peklo, 1913; Jodidi and Peklo, 1929) and on the other it provides additional evidence to prove the symbiotic nature of the fungus; that is, the fungus, in return for the nourishment it receives from the grain, supplies the grain with protein. Quite a large number of

strains of the endophytic fungus have been separated in cultures, a number of them have proved to be physiological strains (Jodidi and Peklo, 1929). The strain which has been called *Lolium fungus* no. 2 may be the apothecial stage of the endophyte (Neill, 1943).

Although endophytic fungi have been isolated from different cereal grains like wheat, barley, rye-grass, etc., the darnel poison which produces the typical symptoms is only present in the hyphæ of the fungus present in the grains of *L. temulentum*. Chemically, this poison is believed to be a pyridine base called temuline. The *Miscara* which was sent to England from Aden for identification and chemical analysis was found to be *L. linicolum* or *L. temulentum* containing temuline.

WHEAT AND LOLIUM

Botanically, lolium, wheat (*Triticum* sp.) and barley (*Hordeum* sp.) are closely related and belong to the tribe *Hordeæ* of the family *Gramineæ*. They differ from each other with respect to the characters of the spikelets and have been placed on that account into separate sub-tribes (Hooker, 1897). As the literature readily available to the toxicologist and public health worker does not contain a good description of the weed, the accompanying photograph (see figures 1, 2, 3 and 4, plate XVIII) of the root, stalk, leaf, ear and grain of wheat and of the weed, side by side, will be found useful in quick identification. The grains of wheat and lolium differ markedly at least in size and can be distinguished as such. There is a sharp microscopical difference between the wheat and lolium starch grains present in the endosperm of each seed. This distinction does not, however, hold good with respect of lolium and barley. Another distinguishing character between wheat and lolium which could be detected under the microscope is the presence of a conspicuous layer of fungal hyphæ between the seed coat and the aleurone layer in lolium seeds which is absent in wheat seeds (Gassner, 1931).

In the present shortage of foodgrains the importance of recognizing the lolium seed, especially in imported wheat, is obvious.

LOLIUM AS AN INTOXICANT

It was reported as early as 1789 (Adam, quoted by Brenchley, *loc. cit.*) that the intoxicating quality of the darnel was known in France, where a narcotic intoxicant liquor used to be produced by brewing barley mixed with lolium. If the intoxicating property of the darnel grains be exploited in future a new aspect of the toxicology of lolium and a new problem in excise will be created.

The writers are indebted to S. N. Bal, M.Sc., Ph.C., Curator, Botanical Survey of India, Indian Museum, Calcutta, for the supply of samples of wheat and darnel seed.

* Excepting barley seeds, which have 2 to 3 layers of aleurone cells, in the cereals the outermost layer of cells of the endosperm get differentiated from the rest as the aleurone layer. These aleurone cells contain special types of protein crystals called 'aleurone grains' which are sometimes associated with complex inorganic salts like double salts of calcium and magnesium phosphate.

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NORMAL BLOOD SEDIMENTATION RATE AND OTHER HÆMATOLOGICAL VALUES IN THE PUNJAB

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THIS work has been undertaken to find out the normal standards of blood sedimentation rate (B.S.R.), total red cell (R.B.C.) count, total white cell (W.B.C.) count, hæmoglobin estimation and packed cell volume in normal healthy Punjabis.

TECHNIQUE

Selection of subjects.—Observations were made on 100 healthy normal medical students (75 boys and 25 girls) between the ages of 18 and 26 years. A thorough clinical examination

of the subjects was done and those indicating actual disease or a suspicion of disease were discarded. The cases showing high B.S.R. were examined by specialists and some were screened and x-rayed so as to exclude the possibility of pathological cases in that way also. Blood samples were collected as described by Napier. Mostly they were drawn before the mid-day meals were taken and all examinations were completed within two hours. The following methods were employed in the determination of the various values:—

(i) B.S.R. was determined by the techniques of Westergren (1921) and Wintrobe-Landsberg (1935).

(ii) Packed-cell volume, total R.B.C. count and total W.B.C. count were determined by the technique as described by Napier and Das Gupta (1945).

(iii) Hæmoglobin determinations were done by using Sahli-Haden hæmoglobinometer.

Deductions of the following were made from the above findings thus:—

(a) Mean corpuscular volume:

Volume of packed cells in c.cm. per 1,000 c.cm. blood ÷ red cells in million per c.mm.

(b) Average corpuscular hæmoglobin:

Hæmoglobin in grammes per litre of blood ÷ red cells in million per c.mm.

(c) Mean corpuscular hæmoglobin concentration percentage:

Hæmoglobin in grammes per 100 c.cm. ÷ Volume of packed cells in 100 c.cm. × 100.

RESULTS

1. *Blood sedimentation rate.*—(a) Westergren technique. The average B.S.R. 1st hour was 7.02 ± 5.97 mm. with a range of 0.5 to 23 mm. in the case of male and 14.4 ± 9.74 with a range of 3 to 27 mm. in the case of female. In the table below the results are compared with those of other authors.

TABLE I

Comparison of results of B.S.R. (Westergren 1st hour) with those of other workers

Number	Author	Values	Male	Female
I	Westergren (1921).	Range	1-3 mm.	4-7 mm.
II	Napier	Range	3-15 mm.	5-40 mm.
III	Present investigation.	(a) Range (b) Average (c) Standard deviation.	0.5-23 mm. 7.02 mm. ± 5.97 mm.	3-27 mm. 14.4 mm. ± 9.74 mm.

(b) Wintrobe method. The average B.S.R. by Wintrobe method was 11.2 ± 9.4 mm. with a range of 0.5 to 30 mm. in the case of males and 24.1 ± 9.74 mm. with a range of 7.37 mm. in the case of females.

TABLE II
Comparison of results of B.S.R. Wintrobe
method with those of other workers

Number	Author	Values	Male	Female
I	Wintrobe and Landsberg (1935).	(a) Range (b) Average	0-9 mm. 3.7 mm.	0-20 mm. 9.6 mm.
II	Napier	Range	2-20 mm.	2-30 mm.
III	Gallagher	(a) Range (b) Average	1-20 mm. 4.7 mm.	
IV	Present investigation.	(a) Range (b) Average (c) Standard deviation.	0.5-30 mm. 11.2 mm. ± 9.4 mm.	7-37 mm. 24.1 mm. ± 9.74 mm.

2. *Total red blood cell count.*—The mean value for R.B.C. obtained in 75 male students was found to be 5.17 ± 0.57 millions per c.mm. The average figures obtained by other authors Sokhey *et al.* (1937), Napier and Das Gupta (1935), Napier and Majumdar (1938) in India

vary between 5.057 and 5.533 millions per c.cm. as against the figures 5.400 and 5.590 millions per c.mm. obtained in U.S.A. and England respectively by Castle and Minot (1936), Whitby and Britton (1939), Price-Jones (1931).

The mean value for R.B.C. obtained in 25 female students was found to be 4.612 ± 0.45 millions per c.mm. The average figures obtained by other authors Sokhey *et al.* (1938), Napier, Neal-Edwards and Das Gupta (1941), Benjamin (1939), Napier and Majumdar (1938), Napier and Billimoria (1937) in India vary between 4.45 and 4.615 millions per c.mm. as against the figures 4.8 and 5.012 millions per c.mm. obtained in Britain by Whitby and Britton (1939) and Price-Jones (1931).

3. *Total white blood cell count.*—The average values of white blood cells were 7 ± 1.78 thousands in males and 6.81 ± 1.85 thousands in females.

4. *Average hæmoglobin value.*—In males were 14.78 ± 1.29 grammes per 100 c.cm. and in

TABLE III

Details of average hæmoglobin values for different populations according to various authorities

Sex	Age	Locality	Economic status	Hæmo-globin, per cent	Standard deviation	Number of cases	Authority
Men	19-30	Bombay	Students	15.37	± 0.96	121	Sokhey <i>et al.</i> (1937).
	25-45	Calcutta	Mixed servants.	14.77	± 1.36	50	Napier and Das Gupta (1935).
Men	25-45	Calcutta	Clerks and doctors.	15.70	± 0.91	30	Napier and Das Gupta (1935).
	Adults	Assam	Coolies	12.62	± 1.41	20	
	"	Cachar	"	12.60	± 1.83	25	Napier and Majumdar (1938).
	"	Assam	"	11.83	± 1.67	24	Napier and Das Gupta (1935).
Men	Adults	Shivrajpur	Coolies	13.74	± 1.79	47	Napier and Sen Gupta (1938).
	"	"	"	12.95	± 1.72	49	
	"	U.S.A.	"	16.00	Castle and Minot (1936).
	"	Britain	"	15.60	Whitby and Britton (1939).
	"	"	"	14.50	Price-Jones (1931).
	"	Punjab	Students	14.78	± 1.29	75	Present investigation.
Women	18-30	Bombay	Coolies	12.99	± 1.10	101	Sokhey <i>et al.</i> (1938).
	14-38	Calcutta	Middle class.	12.63	± 1.01	128	Napier, Neal-Edwards and Das Gupta (1941).
	17-22	Madras	Students	13.73	± 0.93	62	Sankaran and Rajagopal (1938).
	17-30	Delhi	Middle class.	13.11	± 0.81	100	Benjamin (1939).
	Child bearing.	Coonoor (6,000 ft.).	..	15.81	± 2.54	100	Radha Krishna Rao (1938).
		Cachar	Coolies	10.40	± 1.74	25	Napier and Majumdar (1938).
		Assam	..	10.80	± 2.30	20	Napier and Billimoria (1937).
		Britain	..	13.60	Price-Jones (1931).
		"	..	13.70	Whitby and Britton (1939).
Women	18-22	Punjab	Students	13.06	± 1.15	25	Present investigation.
	18-22	Michigan	"	13.76	..	50	Bethell (1936).
Pregnant women.	..	Assam	Coolies	10.70	± 1.60	40	Napier and Billimoria (1937).
"	..	"	"	9.22	± 0.0	228	Napier and Das Gupta (1937).
"	..	"	Obvious anæmics excluded.	9.99	± 1.72	192	" " " " "
"	..	Michigan	"	11.85	..	28	Bethell (1936).
"	..	Coonoor (6,000 ft.).	Ante-natal clinic mixed.	15.52	± 2.52	100	Radha Krishna Rao (1938).

females 13.06 ± 1.15 grammes per 100 c.cm. Since the hæmoglobin estimation in various provinces reported by the various authors varies widely a comparison of the results is given in table III.

Packed-cell volume. The average packed-cell volume was 47 ± 4.17 and 41.8 ± 1.04 for males and females respectively. Volume of the red cells is normally 41 to 45 per cent of that of the blood (Wright, 1945). The values quoted by various authors, however, vary widely.

5. The mean corpuscular volume of this series was 90.7 ± 2.8 in males and 90.6 ± 6.8 in females. Perusal of the literature shows a wide variation of different provinces in India whereas in America and Britain the variation is not so high. For comparison these results are given in table IV.

6. The mean corpuscular hæmoglobin for the Punjab is 28.44 ± 2.02 in male students and 28.17 ± 3.3 in female students and is approximately the same as that found by Napier and Das Gupta in Calcutta. Comparative values are given in table IV.

7. Mean corpuscular hæmoglobin concentration per cent values obtained are 31.44 ± 2.02 in male students and 31.45 ± 4.15 for female students. Comparative values are given in table IV.

Summary

Blood sedimentation rate determinations by Westergren (1926) and Wintrobe methods have been carried out in 100 (75 males and 25 females) normal healthy medical students. Other hæmatological findings like total R.B.C. count, total W.B.C. count, hæmoglobin, packed-cell volume, average corpuscular hæmoglobin, mean corpuscular hæmoglobin concentration per cent, have also been carried out in the same samples of blood. Values for these findings are given in tables I to IV.

There was observed a marked difference in the range of B.S.R. in the two sexes in the present series. The values are 7.02 ± 5.97 in males and 14.4 ± 6.95 in females by Westergren apparatus and 24.1 ± 9.74 in females and 11.2 ± 9.4 in males by Wintrobe method. These figures when compared with the values obtained by workers for European population may be considered to be definitely pathological. They do not, however, differ much from the figures for Bengal.

Normal values of total R.B.C. count, hæmoglobin and mean corpuscular hæmoglobin concentration percentage in the Punjab are low when compared to European figures. Further investigations are in progress in this direction.

TABLE IV

Results of M.C.V., M.C.H., and M.C.H.C. percentage and their standard deviation in various populations according to different authorities

Sex	Locality	Number	Mean corpuscular volume	Standard deviation	Mean corpuscular hæmoglobin, per cent	Standard deviation	Mean corpuscular hæmoglobin concentration, per cent	Standard deviation	Authority
Male	Calcutta	30	90.49	± 7.90	28.53	± 2.31	31.07	± 1.20	Napier and Das Gupta (1936).
"	Bombay	121	87.08	..	30.01	± 0.0	34.54	..	Sokhey <i>et al.</i> (1937).
"	Assam	24	71.29	± 7.04	23.93	± 2.31	32.50	± 3.10	Napier and Das Gupta (1936).
"	Cachar	25	84.93	± 10.78	25.14	± 3.70	29.72	± 2.94	Napier and Majumdar (1938).
"	Punjab	75	90.7	± 2.8	28.44	± 2.02	31.44	± 2.02	Present investigation.
Unspecified	U.S.A.	..	87.00	..	27.5	..	35.00	..	Castle and Minot (1936).
"	Britain	..	86.00	..	29.5	..	34.00	..	Whitby and Britton (1939).
Female	Calcutta	128	86.82	± 7.28	27.42	± 2.89	31.57	± 1.76	Napier, Neal-Edwards and Das Gupta (1941).
"	Bombay	101	88.53	..	29.06	..	32.86	..	Sokhey <i>et al.</i> (1938).
"	Delhi	100	92.7	..	28.78	..	33.58	..	Benjamin (1939).
"	Assam	20	77.30	± 7.70	24.50	± 3.00	31.20	± 1.77	Napier and Billimoria (1937).
"	Cachar	25	82.49	± 12.68	23.42	± 3.10	28.67	± 3.37	Napier and Majumdar (1938).
"	Michigan	50	86.30	Present investigation.
"	Punjab	25	90.60	± 6.8	28.17	± 3.3	31.48	± 4.15	Napier, Neal-Edwards and Das Gupta (1941).
"	Calcutta	64	86.83	± 10.08	26.62	± 3.34	30.57	± 2.1	Napier and Billimoria (1937).
Pregnant Females	Assam	40	72.10	..	23.80	..	32.60	..	Napier and Billimoria (1937).
"	Michigan	28	92.00	Bethell (1936).

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AMOEBIIC ABSCESS OF LIVER BURSTING INTO PERICARDIAL CAVITY

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THE possibility of amoebic abscess of liver bursting into any neighbouring serous cavity is known but bursting of such an abscess into pericardial cavity is not commonly met with.

Case record

A Hindu male, aged 30 years, business man, was brought to me for treatment on 11th April, 1946, and on his request was admitted to hospital the same day. He complained of pain in the epigastrium, duration 2 years, and pain over the left shoulder and upper part of the back of the chest and hiccough for the past 18 days.

Married 5 years back—2 children, both healthy. History of gonorrhœa 12 years back and of syphilis 7 years ago, both treated adequately. No history of definite dysentery but admitted having

passed blood and mucus in stools for few days 8 months back.

He started getting pain in the upper half of the abdomen and along the lower margin of ribs 2 years ago, the pain lasted from a couple of hours to 10 days at a time. He was relieved by treatment. Four months ago he started getting intermittent fever, was treated as a case of pulmonary tuberculosis but fever subsided a month ago. For the last 18 days breathlessness, worse at night, hiccough and pain over the back of the chest made him consult a number of medical men.

On examination: 11th April, 1946.—The patient, emaciated, restless, cyanosed, no œdema, no jaundice, temperature normal, liver enlarged by 2 fingers below the costal margin, hard and tender in the epigastric region. Spleen not palpable. Ascending and descending colon palpable and a bit tender.

Pulse weak, pulsus paradoxus present, veins of neck prominent particularly on lying down. Cardiac dullness increased half an inch to right and half an inch to left of normal area. Heart sounds feebly heard over the mitral area and inaudible over other areas. No murmurs detected. Blood pressure 80/40. Left chest wall slightly œdematous. Left lung—vocal resonance diminished at base, percussion note dull, breath sounds feeble, vocal fremitus diminished and coarse crepitations present over the same area. Right lung—coarse crepitations at base. Friction present over a wide area of lower lobe.

Red blood cell count.—5 millions, hæmoglobin 11.5 grammes.

Total leucocyte count.—28,600.

Differential leucocyte count.—Polymorphonuclears 86 per cent, lymphocytes 13 per cent and eosinophils 1 per cent.

Urine.—Albumin present.

Sputum.—No tubercle bacilli or elastic fibres found.

An x-ray skiagram (see figure 1, plate XIX) taken on 12th February, 1946, showed hilar shadows marked and a somewhat prominent aortic curve. Another skiagram (see figure 2, plate XIX) taken on 12th April, 1946, showed the heart shadow much enlarged in all directions, left dome of liver raised, left side of chest showed fluid. A tentative diagnosis of pericarditis with effusion, abscess of liver and pleural effusion in the left side was made.

A puncture was made in the 8th left intercostal space in the mid-axillary line and sero-sanguineous fluid was found. Another puncture in the 5th left interspace outside the mammary line was made and 40 c.cm. of anchovy sauce pus was drawn. To remove any doubt regarding the site of the pus being the pericardial cavity another puncture was made in the 5th left intercostal space along the left border of the sternum and the needle was pushed inwards, downwards and to the right as far as possible under the sternum and 30 c.cm. of anchovy

sauce pus containing lot of flakes and shreds was drawn. The patient felt comfortable, pulse improved, dyspnoea lessened.

Pus showed no micro-organism and was sterile on culture.

200 c.cm. of 25 per cent glucose in saline was ordered intravenously twice daily and rectal saline with glucose. Emetine gr. $\frac{1}{2}$, strychnine gr. 1/60, digitalin gr. 1/100 twice daily hypodermically.

A surgeon to V. J. Hospital was called in for consultation but the general condition and blood pressure being very poor no surgical treatment was undertaken.

13th April, 1946.—Patient felt better, discomfort over chest less, heart sounds could be heard feebly over all the areas. Kahn and Wassermann reaction of blood negative.

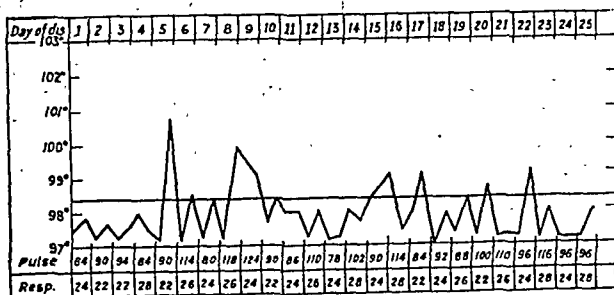
15th April, 1946.—The general condition of the patient a bit better. The surgeon agreed to aspirate and under local anaesthesia 22 ounces of anchovy sauce pus with lot of shreds was withdrawn from the liver by puncturing just below the xiphisternum, and 5 ounces of pale yellow fluid was aspirated from the left pleural cavity.

Pulsus paradoxus disappeared, heart sounds could be heard distinctly over all the areas and no murmurs were heard. Pericardial friction appeared. Impact of cardiac systole could be felt over the 3rd left intercostal space. Pain over the back of the chest and epigastrium much decreased. Hiccough stopped. 300 c.cm. of blood transfusion was given in the evening. This caused great distress to the patient for about 8 hours. He had slight rigor and fever after transfusion.

16th April, 1946.—Patient comfortable in every way although blood pressure remained 80/40.

18th April, 1946.—Vitamin B and vitamin C were started orally in the form of berin and redoxon respectively. Temperature intermittent since 15th April, 1946 (see temperature chart).

CHART



19th April, 1946.—Aspiration of liver repeated by the surgeon and 10 ounces of very thin pus and no shreds were drawn.

23rd April, 1946.—Emetine stopped. Pulse much improved.

24th April, 1946.—General condition better but complained of abdominal distension which was relieved by enema and turpentine stupes, and diarrhoea relieved by sulphaguanidine.

25th April, 1946.—Jaundice was noticed, urine contained bile pigments and bile salts but no albumin. Van den Bergh test of blood gave immediate direct reaction. Icteric index 17. Bile present in stools. Felamine tablets orally were ordered, patient complained of blood and mucus in stools, yatren by mouth was given.

27th April, 1946.—Slight cedema over the feet. Digoxin was started.

29th April, 1946.—Pulse again feeble, signs of consolidation over the right upper lobe, abdominal distension severe, 10 c.cm. of anti-gas gangrene serum was administered as advised by the surgeon.

30th April, 1946.—X-ray skiagram taken on 29th April, 1946 (see figure 3, plate XIX) confirmed consolidation of right upper lobe. Heart shadow enlarged. Sulphadiazine started.

1st May, 1946.—Distension severe, pulsus paradoxus reappeared. Total leucocyte count 11,900.

From 15th April, 1946 to 2nd May, 1946, the temperature was irregularly intermittent, repeated stool examination showed no amœbæ vegetative or cystic forms. Throughout the treatment 200 c.cm. of 25 per cent glucose was given intravenously once or twice a day, supplemented by rectal saline with glucose. Patient was given orange juice, eggs, liver juice, meat extracts, essence of chicken (Brands), milk in the form of junket. He was encouraged to drink fluids but the response was poor.

2nd May, 1946.—Pulse feeble, jaundice more deep, diarrhoea troublesome. Yatren and sulphadiazine stopped. Emetine gr. $\frac{1}{2}$, digitalin gr. 1/100, strychnine gr. 1/60 twice daily hypodermically started and a course of penicillin also. Aspiration of liver at the previous site was done, but nothing could be drawn by the surgeon, then the needle was pushed into the pericardial sac in the ziphisternal notch and 20 ounces of sero-sanguineous fluid were drawn but no pus. The pulse and general condition improved. X-ray skiagram (see figure 4, plate XIX) immediately after aspiration showed that the heart shadow in the upper half has decreased in width but lower half showed fluid level. Right upper lobe opaque and thickened pleura on both sides.

3rd May, 1946.—General condition improved. Abdominal distension much less.

4th May, 1946.—Pulse feeble again, temperature normal, jaundice deepening, abdominal distension marked.

6th May, 1946.—Patient refused food and drink, pulse feeble, drowsiness increased. Emetine stopped, penicillin stopped after three days' course. Patient died at 23.55 hours.

Discussion

The case was undoubtedly one of amœbic abscess of liver which had burst into pericardium. The pus was sterile on culture and showed no micro-organism. The pain in the epigastric region and over the lower margin of ribs taken

in conjunction with x-ray skiagram (12th February, 1946), most probably was due to the liver abscess, it appears that in this case the formation of abscess was spread over 2 years and even up to 12th February, 1946, there was no marked pushing up of diaphragm, the fever which commenced 4 months ago probably was due to liver abscess and as usual the temperature came down to normal when the abscess burst into a neighbouring cavity. The pain over the chest, dyspnoea and hiccough 18 days before admission to hospital marked the time when the abscess must have burst into the pericardial cavity.

The question of open drainage of the pericardium was discussed with the surgeon. It was considered that the general condition and blood pressure were very poor, and decision was deferred till after the aspiration which showed that the pulse and general condition improved, pulsus paradoxus disappeared and the heart sound became audible. This meant that the communication between the pericardial sac and liver abscess was patent and that by aspirating the liver abscess cavity it was possible to drain away the pus from pericardial sac by gravity and assisted by pumping action of heart.

This method was chosen in preference to open drainage of the pericardium to avoid the risk of secondary infection, of prolonged convalescence and, in the presence of liver abscess communicating with the pericardial sac, making an opening by no means at a dependent point.

At the second aspiration the pus was found thinner and at the third aspiration there was no pus and only sero-sanguineous fluid could be drawn.

The increased width of lower half of heart shadow in the last skiagram may partly be due to dilatation of heart and not entirely due to fluid, as the heart sounds could be heard very clearly.

Unfortunately post mortem examination was refused.

The onset of acute jaundice superadded to asthenia was the terminal factor in death. Although the van den Bergh gave a direct positive reaction the presence of bile in sufficient quantity in the stools rules out the possibility of complete obstruction to common bile duct. Jaundice was probably due to degeneration of liver cells.

Summary

1. A case of amœbic abscess of liver which burst into pericardial sac is described.

2. Aspiration of liver compared to open drainage of pericardial sac has been tried as the liver cavity was a more dependent spot and as the communication caused by the bursting of the abscess was patent.

My thanks are due to Dr. Riyaz-i-Qadeer, F.R.C.S., for aspiration of the abscess and pericardial sac and for consultations. I also thank Major S. M. K. Mallick, I.M.S., Principal, Glancy Medical College, Amritsar, for permission to report this case.

[A reference to this subject will be found on page 270 of the June-July 1946 issue of this journal, under the heading 'Amœbic pericarditis'.—EDITOR, I.M.G.]

NEONATAL DEATHS AND STILL BIRTHS IN BOMBAY

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NEONATAL death is usually understood to mean the death of a child in the first month after birth, infant death being death within the first year. The *neonatal death rate* is the number of neonatal deaths per 1,000 live births. The *still birth rate* is the number of babies of over 7 months' pregnancy who are born dead per 1,000 total births.

That the subject of neonatal death and still birth is an important one from the point of view of population figures is brought out by the fact that the neonatal deaths still account for half the total infant deaths, and while, for instance, in England and Wales, the infant death rate has been reduced to half what it was in 1900, the neonatal death rate has shown little or no decrease. What is true for England and Wales applies in this respect more or less to all other civilized countries during the last forty years. 1943 figures for England were: Infant death rate 49 per 1,000 live births, neonatal death rate about 25 per 1,000 live births.

Corresponding figures for the whole of India are given as infant mortality 165/1,000 or about 83.5/1,000 as neonatal mortality (Bozman, 1945).

Since most neonatal deaths occur during the first week of life (1/5 occur in the first 24 hours) the figures of the Bai Motlibai and the N. M. Wadia Hospitals, two of the biggest maternity hospitals in Bombay, may be taken as a very rough guide to the position as regards neonatal deaths where skilled attention is available. Patients usually stay in these hospitals 7 to 10 days after delivery.

When these figures are considered with the total number of babies born of viable age (i.e. total births) at these two hospitals, in one year out of 8,542 such babies 1,058 were lost either before birth or during the first ten days of life—nearly 1 in 8 of all births or 12.5 per cent.

I have taken the still births into consideration here since it is well known that most of the causes that lead to still births also produce neonatal deaths, and the two conditions must therefore be considered together if any improvement in the figures for either is to be expected.

We may therefore take this figure of 12.5 per cent (1 in 8 deliveries) as the combined loss by still birth and neonatal death in the first 10 days as a rough estimate for two leading Bombay hospitals serving the poorer classes.

Let us see how they compare with figures from the latest Public Health Report for the Province and City of Bombay, 1943.

At the outset we must admit that we are dealing with very rough figures here, as, owing to lack of staff and deficient registration, births, especially, are often not recorded. The report mentioned, for instance, notes that 2,000 births

TABLE I

1943	Number of live births	Number of babies dying in hospital	Deaths per 1,000 live births	Still births	Still births per 1,000 total births
N. M. Wadia Hospital ..	5,741	336	58	348	57
Bai Motlibai Hospital ..	2,248	169	78	205	83

and 459 deaths were detected by the public health authorities as not having been registered in 1943 in Bombay Province; many more no doubt escaped detection altogether. But bearing in mind these limitations we find that in the whole province where the poor form the vast bulk of the population :

1. *The still births* are stated to be 7 per cent of the live births. The *still birth rate* would thus be 65 per 1,000 births.

2. *Infant mortality rate* was 160 per 1,000 live births (192 in urban and 147 in rural areas). Of these 38 per cent died under one month, 21 per cent under one week.

3. *Urban neonatal death rate* would therefore be about 38 per cent of 192, i.e. 80 per 1,000—a figure somewhat better than that of the two hospitals above, which only include the majority (first 10 days) of the neonatal deaths and deal very largely with complicated pregnancy and labour.

Now let us compare these two sets of figures for Bombay Province and for a rather special section of the poorer classes with those taken from two Bombay nursing homes and from the British Families Hospital, which were kindly supplied to me by the superintendents concerned. All three places serve the more wealthy of the population of all communities. The staff of doctors and nurses working there are very varied and are certainly no better than those of the two Bombay maternity hospitals already mentioned. In many cases the doctors are the same. But all the patients have some antenatal care.

Taking the two nursing homes and hospital together over the four years 1941-44 in order to get sufficient material we get the following figures :—

The figures taken are of course smaller than those for Bombay City and Province and can themselves well be improved, but at least they do show what can be done even in the tropics with ordinary medical and nursing care in the case of the better nourished and more intelligent members of society.

The point brought out by these figures then is not so much that better trained and more plentiful staff is required to reduce materially the appalling wastage of potential citizens, as that a higher standard of education and livelihood for the population as a whole is more necessary. They should be educated to the point of *insisting* on proper cleanliness and care in pregnancy and child birth, and seeing that they get it. That they do not so insist at present is due largely to their husbands and fathers who, with their better education and knowledge, still do not dare to stand up to the orthodox old women who rule their homes.

It is quite true that better antenatal care, better midwifery and better postnatal care will save mothers and children who would otherwise be lost, but the numbers that can be so saved are few compared with the numbers that could be saved by a general rise of living and educational standards throughout the country.

This statement is borne out too by an analysis of the causes of these still births and neonatal deaths as far as they can be ascertained. Both sets of deaths may be considered together, as causes which produce still births are the same as those which produce deaths in the first few days of life. After the first few days acquired infections such as respiratory, gastro-intestinal and skin infections become increasingly important.

TABLE II

Names	Total number of births	Maternal deaths	Neonatal deaths	Neonatal deaths per 1,000 live births	Still births	Still births per 1,000 total births
St. George's Nursing Home St. Elizabeth Nursing Home British Families Hospital	1,214	3	13	11	25	21

It will be seen that the neonatal death rate is 11 per 1,000 live births compared with 58 and 78 for the two large Bombay hospitals and 80 for Bombay Province as a whole, and the still birth rate 21 per 1,000 births (Bombay Province well over 70). Total wastage of foetal and neonatal life is 3.1 per cent compared with 12.3 per cent of the two big Bombay maternity hospitals for poorer patients.

In all the series of cases from every hospital and nursing home without exception *prematurity* is the chief cause of both still births and neonatal deaths. This is only to be expected, as a premature child is less able to withstand any trauma or difficulty associated with its birth, and also less resistant to infection and changes of temperature and has more difficulty in getting sufficient nourishment than a full-time child. So

that even when the cause of death is returned as due to 'intracranial hæmorrhage', 'asphyxia', or 'gastro-intestinal infection' for instance, the underlying predisposing cause is often prematurity.

It will suffice if we take the figures of the Bai Motlibai Hospital for one year to illustrate this point. In 1941 for instance there were 97 still births and 143 neonatal deaths in hospital out of 1,991 confinements—a total loss of 240 babies. Of these 191 were prematures or nearly 79 per cent.

The figures of that year also illustrate the value of *antenatal care* (or possibly the value of education or common sense in mothers who bother to attend antenatal departments).

There were 1,255 'booked cases' who did so attend at least once and 736 'emergency cases' (37 per cent) who had not made even one visit to the antenatal department.

The still births and neonatal deaths in the two groups are shown in table III.

TABLE III

Sl. No.	In booked cases	Percentage of total booked cases	In emergency cases	Percentage of total emergency cases
Still births	24	1.9	73	9.9
Neonatal deaths	38	3.0	105	14.4

It will be seen that the rate for the more ignorant or lazy emergency cases who never attended the antenatal department is about five times as high in both still births and neonatal deaths as it is for the more careful members of society.

Figures from other years at this hospital and from the N. M. Wadia Hospital tell the same story. In fact, from the table above it will be seen that for *booked cases* the still birth rate and neonatal death rate 1.9 per cent and 2.9 per cent of confinements are more nearly comparable with that of the better class hospital and two nursing homes quoted above, whose figures were respectively 2.1 per cent still births and 1.1 per cent neonatal deaths.

Compared with these two main causes of loss of babies—*prematurity* and *lack of antenatal care* and all that they signify as to the level of education, living conditions including proper hygiene in its widest sense, etc.—the other ultimate causes of loss pale into relative insignificance.

They are much the same as are found in English and American statistics (Adair, 1940) roughly about 30 per cent due to birth accidents and trauma (placenta prævia, accidental hæmorrhage, birth injuries, breech deliveries, prolapsed cord, etc.); 30 per cent due to disease of the mother (such as anæmia, fevers, nephritis,

toxæmias of pregnancy, etc.); 30 per cent due to postnatal infections (gastro-intestinal, respiratory or skin diseases). The remaining 10 per cent are due to developmental defects or often no cause can be found to account for them even on post-mortem examination.

The point is that they are all uncommon compared with the vast numbers of deaths due to prematurity and lack of antenatal care. If we want to make any marked improvement in our figures we must first of all concentrate on these two chief causes.

Antenatal care.—Let us take this question first, though it is to some extent mixed up with that of prematurity in that lack of the one may lead to the other.

If every pregnant woman had even one thorough examination during the last two months of pregnancy what a difference it would make to the safety both of herself and her child! Actually, though monthly visits from the 2nd month and fortnightly or weekly visits from the 8th month are desirable, and though patients are told this, few from the poorer classes come more than once or twice in the whole of pregnancy. And often then they come only in order to get an antenatal card without which they fear they may be unable to gain admission to hospital when labour starts. Why?

It is easy to put this down to lack of education and lack of knowledge, and no doubt to a great extent it is true. But we as doctors should do all in our power to make these visits easy and attractive. I would even go so far as to have a film show or entertainment provided free now and then for mothers who qualify by so many regular attendances at the antenatal department.

But even short of such extravagant notions, we could do a lot more to make these visits more popular.

Some suggestions.—1. *The times* of the antenatal examinations should be such as would suit the convenience of the majority of mothers and fit in with their own time tables.

2. *The staff and equipment and examination couches* should be sufficient to avoid long waits.

3. *The teaching of students* should be carried out only on those patients who are willing to be used for teaching purposes. The number of students allowed to examine each case to be limited to two at the most.

4. *A separate room staffed only by women doctors and women students* should be set aside for those who prefer to be examined by women. At present at the Bai Motlibai Hospital two days a week are devoted to such patients but they are apt to forget which two days those are.

5. *The waiting rooms* could be made larger and more attractive with comfortable clean chairs, cushions, curtains, pictures, etc. Short talks (10 to 15 minutes) could be given to these women in their own language by a student, nurse (if one could be spared!) or welfare worker on some subject to do with maternity or

child welfare. Patients should not be forced to listen to these if they don't want to.

On some such lines lies our hope of inducing the more ignorant mothers to attend for antenatal examination.

Premature births.—This is a more difficult subject, and we are handicapped by lack of exact statistical knowledge of the causes.

It is well known that in a healthy woman and even one who is suffering from toxæmia of pregnancy induction of labour even near term by medical means may be extraordinarily difficult, even when reinforced by drives over bumpy roads, etc.

And yet in others, apparently no less healthy, a pregnancy may terminate prematurely from very trivial trauma or unwonted exertion, or even with no ascertainable cause.

And these two types of pregnancy may occur in the same woman, so that a series of normal full-term deliveries may be interrupted by a premature birth.

It would seem, therefore, that we have still a great deal to learn about the causes of premature labour, and a list of diseases and obstetrical conditions associated with it, though helpful, must not blind us to the fact that in very many premature labours no sufficient cause can be found in the shape of maternal or foetal abnormalities or presentations.

In spite of this lack of knowledge in all cases some conditions are well authenticated predisposing causes of premature labour and a list of the commoner ones is given below:—

CONDITIONS PREDISPOSING TO PREMATURE BIRTH

A. Obstetrical

Over-distension of the uterus combined with the lack of support to the amniotic sac in the regions of the os.

1. Twins—especially with non-engagement of a head.
2. Malpresentations and monsters.
3. Hydramnios—even in minor degrees.
4. High amputation of the cervix.
5. Multiparity with a partially dilated cervix (especially when combined with twins, malpresentations or hydramnios).
6. Placenta prævia.
7. Cervical fibroids.
8. Trauma.

B. Maternal disease or debility

1. Rapidly repeated pregnancies.
2. Extreme youth of the mother (possibly connected with over-distension of the uterus and tense abdominal wall).
3. Hard physical work and lack of rest during last 3 months of pregnancy.
4. Chronic nephritis, toxæmias, accidental hæmorrhage.
5. Fevers (which in some cases first kill the child).
6. Anæmias and avitaminoses.
7. Anxiety, fear, mental shock.

8. Drugs and poisons (such as chronic lead poisoning).

9. Syphilis (only about 5 per cent of all premature births).

C. Causes in the fœtus or membranes

1. Monsters (mentioned above).
2. Syphilis.
3. Placenta prævia or accidental hæmorrhage.
4. Death of the child from any cause mentioned above.

It will be seen that often several of these causes may be working together in any given case and that certainly applies to most of the patients from the poorer classes in Bombay.

I have no actual figures of the proportion of premature to full-term births. In the absence of reliable menstrual histories and of any fixed standard as to the dividing line between what may be considered a full-term child and what a premature one, such figures are subject to error. I have taken any child of Indian parents weighing less than 5 pounds at birth to be premature and less than 5½ pounds for European parents. (At the Bai Motlibai Hospital under 4 pounds is taken to be a premature child. Such children form 8 to 10 per cent of all live births there.)

My impression is that premature births are several times as common in patients from the poorer classes as they are in those from well-to-do families.

As regards *prevention* of these premature births I think we should start at the beginning by (1) *voluntary limitation of the size of the family* and (2) *better spacing of pregnancies*. This is a matter of educating wives and their husbands to understand that a woman who already has a large family of children born one after the other at very short intervals, whom she has to look after with no domestic help, is not likely to be able to bear more children without danger unless she has adequate rest for recuperation. Birth control clinics are badly needed for these women.

Next *general hygienic measures* and welfare work in its widest sense for expectant mothers are urgently required. Expectant mothers should be exempted from work at the mills, etc., for the last few months of pregnancy and their pay given them *in kind*—in the shape of extra milk, vegetables, vitamin concentrates, iron, etc.

Crèches and child welfare centres and kindergarten schools should be made more numerous and attractive and here the younger children could be sent daily so as to lighten the tasks of these mothers in their homes.

These benefits should be contingent on the mother's regular attendance at a proper antenatal clinic, where many of the more obvious causes of premature labours can be diagnosed and appropriate treatment given.

For *treatment of the premature baby* not much can be added to what is already well known (but

seldom carried out entirely) as regards these children.

Their chief needs are rest, a warm equable temperature, frequent small easily digested feeds and water and freedom from risk of infection. Every textbook of midwifery gives directions as to how these needs are to be met.

As regards conditions in Bombay I would merely add two points:—

(i) We should have at least two fully air-conditioned rooms in each hospital for these children—one kept at about 90°F. for new-born prematures and one at about 80°F. day and night with that humidity which is found by experiment to suit these babies best.

(ii) An adequate staff of special nurses for these rooms. They must work here and nowhere else in the hospital. They should work only in special overalls and masks and keep themselves free as far as possible from all infectious and respiratory diseases or risk of contacts with those suffering from them. They should at once report the onset of a cold or sore throat in themselves and be transferred to work in another ward till fully recovered.

Such a nursing staff by constant practice would get expert at dealing with these delicate babies, handling them as little as possible for feeds or nursing purposes and the results of their care should show a marked fall in the death rate of these children.

The children should be kept in hospital till they weigh at least 7 pounds.

One may think that all this is a Utopian dream and would cost too much money, and certainly it will cost some. But there is no reason why it should not be tried out in at least one of our city maternity hospitals as a sort of 'Pilot Plant' for a few years. It is at any rate certain that some such scheme, as I have outlined, is required if the appalling figures for neonatal deaths are to be much improved.

Summary

1. The neonatal death rate and still birth rate for some hospitals and nursing homes in Bombay are discussed and compared with corresponding figures for England and India as a whole.

2. Causes of the high rate in the poorer classes in Bombay are outlined and some remedial measures suggested, especially with a view to preventing premature births.

My thanks are due to the Superintendents of the J. J. Group of Hospitals, the N. M. Wadia Hospital, St. George's Hospital, the Officer Commanding British Military Hospital, Colaba, and the Sister Superior, St. Elizabeth's Nursing Home, for permission to use figures from their hospitals and to those in charge of the maternity departments of these institutions who very kindly supplied them.

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A NEW OIL MEDIUM FOR ENHANCEMENT OF GROWTH OF THE MALASSEZIA AND SUBSEQUENT STUDY OF SEROLOGICAL REACTIONS AND PATHOGENICITY *

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THE organisms under the genus *Malassezia* were first successfully cultivated by the author in 1927 (Acton and Panja). Subsequently, the detailed work on the *Malassezia* was published in 1928 (Panja). Ota and Huang (1933) confirmed the author's work and Dodge (1936) accepted his classification of the *Malassezia* in preference to the old classification of the *Pityrosporum*, Sabouraud, 1895.

The colonies on glucose or maltose agar media were pin-point and scanty and formation of mycelium was rarely seen. For experimental and serological works also, such scanty growths were unsatisfactory. Hence a further search was made for a better medium which would yield copious growth on subculture.

It was found that by using cocoanut oil on the scalp affected with dandruff although dandruff scales tended to disappear, the *Malassezia ovalis* (bottle bacillus of Unna) multiplied in the scales. This suggested the idea that the oil might serve as an enrichment medium for growth of the above organism. The new medium is simple and consists of nutrient agar either plain or incorporated with either glucose or maltose or glycerine. To such an agar slope, a little sterilized cocoanut or olive oil is added to coat the surface of the slope. The *Malassezia* grow well on such a medium as opaque, creamy and large colonies like those of a yeast in 1 to 3 days. Growth is more profuse in the oil at the bottom of the slope than on the upper part. Hence in order to have a uniform profuse growth all over the surface it is necessary to spread the oil from the bottom all over the surface once every day by tilting the slope. It is important to note that if oil alone is used there is no growth. If oil is poured on the fine colonies of the *Malassezia* on a solid medium, the colonies with which the oil comes in contact assume a large, thick and creamy appearance in 24 hours whereas the untouched ones are unaffected (see figure, plate XX). This suggests that the oil probably forms a thick opaque coating on the organisms. But microscopically the organisms are found really to multiply in the oil the latter in conjunction with agar acting as a stimulant but by itself being inactive. On treating the oil grown cultures with ether also, no evidence is available that the oil forms a thick coating on the organisms. If the oil is

* This paper was read at the meeting of the Indian Science Congress Association held at Benares in 1941.

added to a tube of glucose broth and then the organism is grown with occasional shaking of the medium, thick growth takes place in the oily top layer only and no macroscopic growth is seen in the subjacent broth medium. With some strains of the *Malassezia*, no mycelia are found on plain glucose agar culture in 3 weeks, but in the oil medium on glucose agar mycelia appear in 3 days. Several oils were tested for growth of the organisms. Fixed oils, such as olive oil, coconut oil, almond oil, hydnocarpus oil, *til* oil, *neem* oil, castor oil, and *ghee* (clarified butter), all stimulate the growth but oils containing volatile oils, such as eucalyptus, lemon grass, santal and mustard, completely hinder the growth. It is interesting to note here that the oils, such as olive, coconut, santal and *neem*, do not stimulate the growth of *Epidermophyton inguinale* but hinder it. Coconut oil contains 55 per cent lauric acid and 10 per cent oleic acid; lauric acid inhibits growth whereas oleic acid favours the growth of the *Malassezia*. The following shows the result of an experiment, + indicating growth :—

	Olein	Laurin	Palmitin	Stearin
<i>M. ovalis</i>	+++	±	+++ (pale orange coloured growth).	—
<i>M. furfur</i>	+++	+	+++ (pale orange coloured growth).	—
<i>M. tropica</i>	+++	+++	+++ (pale orange coloured growth).	—

There are only a few strains of the *Malassezia* which grow well on the modified Petroff's medium (Panja, 1928) but grow very feebly or do not grow at all on the new oil medium. Instead of the oil, butter or *ghee* can be used on the solid medium. Growth occurs well on such a medium but the medium is not nice-looking and clean and colonies are not so well visible as on the oil medium.

Serological reactions

As the organism grows profusely on the oil medium, a thick suspension of antigen was easily prepared and injected into rabbits. Agglutination tests were not satisfactory as the suspension was granular. An antigen for precipitation was more easily prepared by boiling a thick suspension in distilled water for 2 hours. The supernatant clear fluid was used undiluted as an antigen.

Pathogenicity tests

A culture of *M. furfur* from the oil medium was used.

Mouse—Thickening at the site of a hypodermic injection; remains alive after a big dose of intraperitoneal injection. P. M. 2 weeks after injection—nodule in the parietal wall of

abdomen; whitish nodules in the omentum; intracellular organisms present in the peritoneum as well as in the nodules.

Guinea-pig—Intradermal injection; redness and slight swelling after one day. A flat fibrous nodule after 10 days.

Rabbit—Thick and live suspension intravenously; no death.

Man—Dermally; redness and very slight oedema in 2 days. Scraping shows *Malassezia*.

Summary

1. A new oil medium has been devised for enhancement of growth of the *Malassezia*. It consists of an ordinary nutrient agar or glucose or preferably maltose agar with a fixed oil, such as coconut or olive oil, put on the surface. Fine pin-point colonies of the micro-organism assume the colony-size of an ordinary yeast in 24 to 48 hours.

2. Such a luxuriant growth is most suitable for the study of morphological variations, biochemical reactions, immunological experiments and pathogenicity tests.

3. A precipitating antigen has been prepared by boiling the organism in distilled water.

4. The organism is non-toxic to laboratory animals.

5. Volatile oils inhibit the growth of the *Malassezia*.

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USE OF PENICILLIN IN RAT AND HUMAN LEPROSY*

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In October 1944, concentrated penicillin was prepared in my laboratory. It was tested on the standard strain of *Staphylococcus aureus* and found highly potent. Three white rats, each weighing about 100 grammes, were inoculated intraperitoneally with 0.5 c.cm. of fresh rat leprosy material. A subcutaneous injection with 0.5 c.cm. of the material was also given in the groin at the same time. From the second day onward after inoculation with the leprosy material penicillin was given intraperitoneally, 400 units, twice a day for seven consecutive days and then once a week for eight to nine weeks more. Subsequently, penicillin prepared

* This paper was read before the Indian Science Congress Session held at Bangalore in January 1946.

by Messrs. E. R. Squibb and Sons, U. S. A., was available and tried on another group of three rats in the same way. The experiments were repeated on another group of white rats in November 1944. Control with rat leprosy material alone and penicillin alone were also put up. Control animals receiving rat leprosy material alone were killed after sixteen to eighteen weeks. Characteristic lesions in the spleen and omentum showing abundance of leprosy bacilli were found. No animals died receiving penicillin alone. Penicillin-treated animals died after sixteen to twenty weeks showing more marked lesion; in the spleen, liver and omentum and abundance of leprosy bacilli. It was thus seen that penicillin used as above had no effect in controlling and curing rat leprosy. In fact, the drug appeared to hasten the death of the animals and favour the multiplication of the bacilli giving rise to more characteristic lesions in the spleen, liver and omentum.

Penicillin was also tried on human leprosy. One nodular case with an isolated nodule in the ear received local intradermal injections. Four cases showing hypopigmented or erythematous patches and thickening of adjoining nerves received local intradermal injections into the patches as well as subcutaneous injections around the thickened nerves. The dosage employed was 400 to 1,200 units at an interval of three to four days lasting for about a month. No improvement in the patches, thickening and tenderness of nerves and disappearance or diminution in the number of bacilli in the nodule were noticed. As there was no improvement, some of the patients discontinued the treatment. Penicillin had evidently no beneficial effect on human leprosy.

My thanks are due to Mr. S. K. Ghosh, my chemist, who prepared the penicillin for me and concentrated it.

OCCURRENCE OF *BACT. ALCALIGENES* SP. IN DUCK EGGS

By J. A. IDNANI

and

C. SEETHARAMAN

Imperial Veterinary Research Institute, Mukteswar

INVESTIGATIONS which led to the discovery of the organism under review were primarily directed towards propagation of the virus of Ranikhet disease of fowls in duck embryos. A flock of twelve ducks was purchased from the plains and reared at Mukteswar. They were housed in one pen, containing a tank. The diet consisted of bran, crushed maize, paddy and wheat. Eggs were collected every morning and set in ordinary egg incubators. Development of embryos was on the whole satisfactory and the work progressed uneventfully. The following year, another twelve ducks were imported and reared along with the first lot. This time

about 50 per cent of embryos were found to be dead at the first candling on the ninth day and 25 per cent failed to develop. This mishap could not be attributed to the drakes since there were several of these in the flock.

Bacteriological examination of a few dead embryos revealed an organism in pure culture with the following characters: Short Gram-positive rods with rounded ends, arranged singly, non-motile, growing well on plain agar and on blood agar. On agar plates, colonies were circular, grey in colour, differentiated into central and peripheral portions, and developing a lemon-yellow colour after 24 to 48 hours at room temperature. In plain broth there was surface growth, indicated by a whitish ring in contact with the glass, and a viscid sediment, partially disintegrating on shaking. In gelatine stab, growth occurred without liquefaction. Fermentation and biochemical reactions were as follows: No change in glucose, maltose, lactose, sucrose, mannitol or salicin. M.R. and V.P. reactions negative; no reduction of nitrate and no indol production. There was production of H_2S and ammonia; litmus milk was rendered alkaline.

This organism was identified according to Bergey (1939) as belonging to *Bact. alcaligenes* sp., probably *Bact. alcaligenes metalcaligenes* (Castellani). Braga (1938) has recorded the occurrence of *Bact. alcaligenes* sp. in hens' eggs and Valle, Braga and Wey (1938) have recorded deaths in young ducks due to infection with *Bact. alcaligenes*. Chaudhuri (1944) has recorded the occurrence of a typhoid-like fever in human beings due to *Bact. alcaligenes*. He uttered a note of warning against a symptomatic diagnosis of typhoid fever and stressed the necessity of conducting agglutination tests with sera from affected cases before making a diagnosis. Chaudhuri detected six cases of what appeared to be typhoid which harboured the organism under review. *Bact. alcaligenes* is a normal inhabitant of the intestinal tract which, under certain circumstances, is apt to invade the blood stream. In the duck or hen, the organism probably lodges in the ovary, thus passing into the egg.

Efforts directed at isolating ducks laying infected eggs were unsuccessful. Later, agglutination tests of sera of all ducks were undertaken. In two out of twenty ducks, titres up to 1:50 were obtained. Within a month both these ducks died but cultures from their blood and ovaries failed to demonstrate organisms.

This organism appears to be important from the public health point of view, in that it is likely to be transferred to human beings through infected eggs. It may also hamper the development of a poultry farm, should infected hens or ducks happen to be present. Bacteriological examination of eggs is therefore suggested if the occurrence of many infertile eggs or early deaths in embryos could not be traced to any known reasons.

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A Mirror of Hospital Practice

A CASE OF PETITS EVENTRATION OF THE DIAPHRAGM*

By J. A. SHORTEN, B.A., M.B., M.R.C.P. (Lond.), F.F.R. (Lond.)

LIEUTENANT-COLONEL, I.M.S. (Retd.)

PATIENT, a man of 34 years of age, had been complaining of indigestion for some years. This was associated with gaseous distension in the left hypochondrium and occasional vomiting. Patient presented himself in the first instance for x-ray examination of the gall-bladder.

During fluoroscopic examination it was noticed that the fundus of the stomach, filled with gas, extended high up into the left lung field and, while the movements of the diaphragm on the right side were free, there was little movement on the left side, and that was of a paradoxical nature (see figure 1, plate XX).

A postero-anterior skiagram of the chest showed the fundus of the stomach distended with gas reaching up to the fourth costal cartilage. The apex of the left ventricle and some lung markings could be seen through this. The contour of the dome formed a regular arc right across the hemithorax. The mediastinal contents were displaced to the opposite side.

A barium meal showed the following additional points:—

1. Rotation of the stomach between its fixed points, the cardia and pylorus, causing biloculation (see figure 2, plate XX).
2. Presence of the splenic flexure, filled with barium emulsion and gas, in the dome at 5 hours after ingestion of the meal (see figure 3, plate XX).

According to Woodburn Morison the contour of the diaphragm, its position, and movements are constant, and cardinal. Diaphragmatic hernia presents a different appearance.

The hernial sac produces a hump in the diaphragmatic outline and some portion of the diaphragm with normal movements is usually visible.

Temporary elevation of the diaphragm due to gaseous distension is not usually so marked and the movements are normal.

A suggestion that appearances were due to a congenital cyst of the lung was ruled out on several grounds. For instance, the barium meal showed that the dome was occupied by the distended gas bubble of the stomach and the splenic

* Read at the monthly clinical meeting held at the School of Tropical Medicine, Calcutta, in January-February 1946.

flexure of the colon, and the passage of a stomach tube caused temporary marked reduction in size.

EFFECT OF INTRAMUSCULAR PARALDEHYDE IN CHOREA

By P. N. LAHA, M.D. (Patna)

(From the Department of Diseases of Children, Medical College, Agra, U. P.)

VERY active or heroic treatment has no scope in chorea. It has no specific remedy, nor has any drug been shown capable of preventing carditis—the most unwelcome complication of the disease. Sedatives are usually given to relieve the violence of choreic movements.

In the case reported below paraldehyde was used by the intramuscular route as a sedative.

P., Hindu female child, aged 9 years, was admitted to the Children's Ward. Complaints:—Choreic movements, duration 10 days.

On examination.—Violent choreic movements involving the whole body. Temperature normal, pulse rate 90, and irregular respiratory movements with an average rate of 20 per minute. Tonsils enlarged and epitrochlear glands palpable. Tendon jerks diminished. Abdominal reflex lost in all quadrants. Babinski plantar response flexor. A soft systolic murmur heard at the apex. Pulmonary second sound accentuated. Other systems clinically normal.

Investigations.—Blood: red cells 4,100,000 per c.mm.; white cells 6,900 per c.mm.; hæmoglobin 12 gm.; polymorphonuclears 70 per cent, lymphocytes 27 per cent, large mononuclears 1 per cent, eosinophils 2 per cent; sedimentation rate (Wintrobe) 36 mm. during first hour. Wassermann reaction—negative. Stool and urine showed no abnormal findings.

Progress and treatment.—The patient was given complete rest in bed and a liberal diet. Three c.cm. of paraldehyde were injected by the intramuscular route every 4 hours for 5 consecutive days and nights. No other medicine was given by any other route. It was observed that for about 2 to 3 hours after each injection of paraldehyde the patient used to be completely free from choreic movements which reappeared after the above-mentioned period. But she developed 2 abscesses one on each thigh at the sites of injection. They healed up quickly. From the sixth day the patient was put on aspirin 10 grains three times a day. After 24 days the patient became free from chorea.

Before being discharged from the hospital she had normal pulse rate, normal tendon jerks and abdominal reflex, normal pulmonary second sound, no murmur at the apex and the following blood picture: red cells 4,400,000 per c.mm.; white cells 13,200 per c.mm.; hæmoglobin 13 gm.; polymorphonuclears 65 per cent, lymphocytes 31 per cent, large mononuclears 1 per cent, eosinophils 3 per cent; and sedimentation rate (Wintrobe) 12 mm. during first hour.

Conclusions

1. Intramuscular paraldehyde is effective in abolishing choreic movements for a limited period.
2. It does not cut short the course of the disease.
3. It may produce abscess at the site of injection.

My thanks are due to Major-General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College, Agra, for his very kind permission to publish the report of the case. I express my appreciation of the services of my house-physician Dr. B. P. Kacker in treating the case.



Fig. 1.

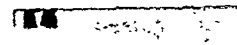


Fig. 2.

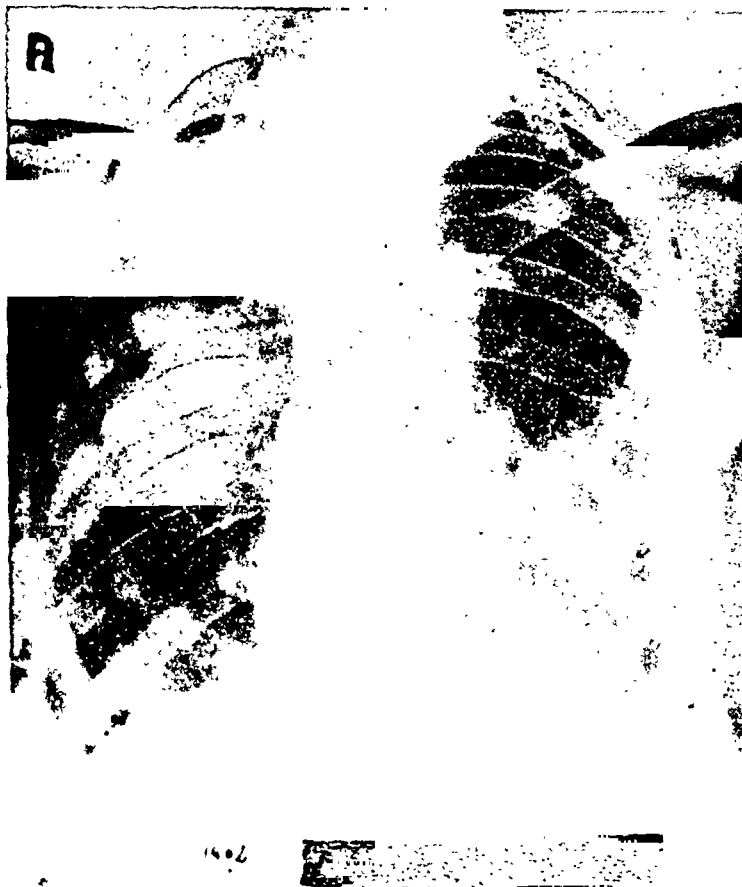


Fig. 3.



Fig. 4.

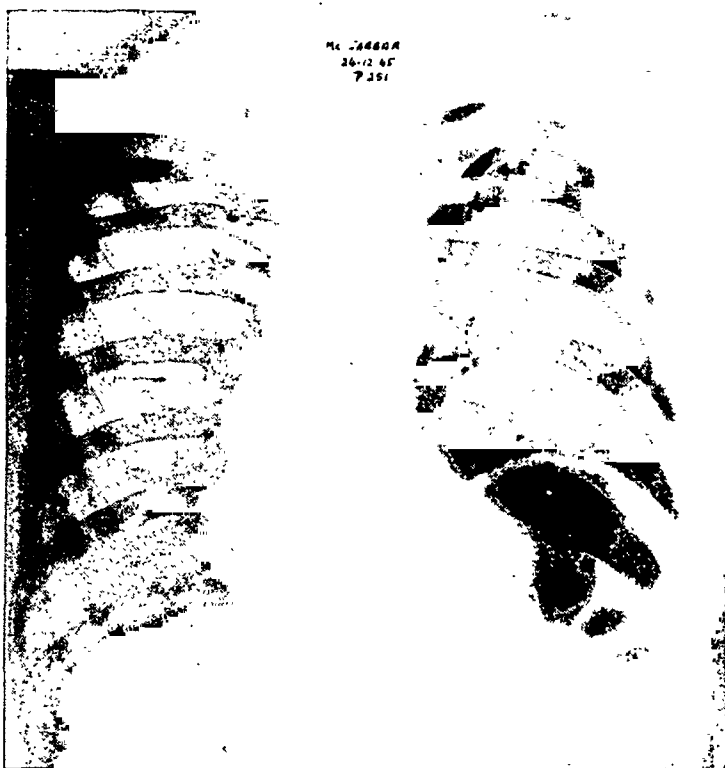


Fig. 1.—Chest P.A. at 2 metres showing elevation of the diaphragm, with lung markings and the apex of the heart seen through the gas bubble, also displacement of the mediastinum and complementary emphysema of the left lung.

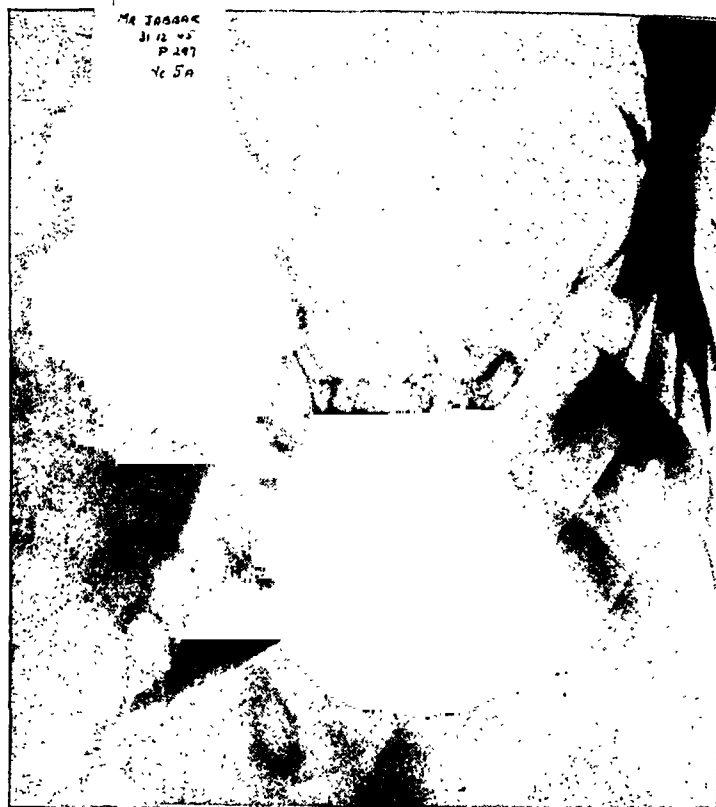


Fig. 2.—After a barium meal showing rotation and biloculation of the stomach.



Fig. 3.—Showing the contents of the dome, the distended gas bubble of the stomach and the splenic flexure of the colon.

A NEW OIL MEDIUM FOR ENHANCEMENT
OF GROWTH OF THE MALASSEZIA, ETC.:
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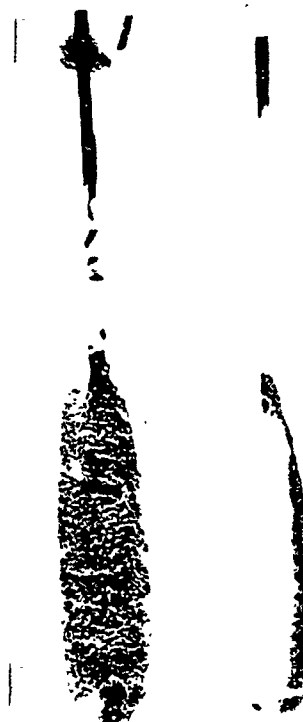


Figure showing luxuriant growth of Malassezia on the new oil medium (Panja)—left hand side. Fine colonies on a medium without the oil—right hand side.

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Indian Medical Gazette

AUGUST

COMFORT FOR THE MIDDLE-AGED

MIDDLE age is the choicest section of the human span of life. In it one can dream dreams and also see visions. Yet the section has received scant consideration in the tabulation of ages by Oxford and Bacon (Shakespeare for the uninformed or the unconvinced).

The undoubted increase in the expectation of life after World War I has probably increased the numerical strength of middle-aged men particularly. It is now up to them to raise the age of their compulsory retirement into old age by retaining their activity and consequently increasing their efficiency with the aid of extra comfort.

The comfort of comforts in this age comes with the removal of restraint of tight clothing. When the state of nourishment of the body generally and of the abdomen particularly has reached a certain point, pressure on the neck and the abdomen must be liquidated.

The collar should be suitably shaped: simple looseness will not do. If a tennis shirt is worn during the day in summer (there is no reason why it should not be worn on most days in summer) the tie (preferably a bow tie, like the one worn by Winston Churchill) should be removed in the office. Incidentally, the shirt needs making to measure as much as other clothes. An ill-fitting shirt with transverse and oblique folds moving across (instead of along) the trunk, with every change of posture and position, produces a sensation akin to that produced by vermin.

The top of the trousers, worn with braces, should sit where it moves least with breathing, after a meal. To facilitate further its sitting, the back should be slit. The braces should be selected or made specially to suit the size. They are quite easy to make and when made of drill are washable. (The six narrow strips which hold the buttons of the garment can be buttoned to the rest of the braces with rubber or soft cotton buttons.)

The jacket should have side slits 2 to 4 inches long and a link button in front (in addition to the other buttons, preferably two only). A sports jacket should have a box pleat at the back (like the one in a bush shirt) and so placed that on folding the arms in front no pressure is felt at the back. The sleeves should be so made that all the buttons at the wrist can be undone. The swing of the arm, then, does not meet any resistance whatsoever in walking. It is surprising how resistance in

walking can produce a feeling of frustration in a man who by virtue of his richness in life's experience is as often as not pre-occupied even out of office. For hot weather a sleeveless jacket is to be preferred to a bush shirt. An old jacket with the sleeves removed, armholes widened and collar renovated suffices. It has all the pockets for all the necessities of a busy life—glasses, watch, pocket book, pen, pencil, wallet and even implements of one's calling like the thermometer and the stethoscope. Most of these objects are spoilt by perspiration if carried in the pockets of a bush shirt and cannot, besides, be carried comfortably, in as much as the bush shirt cannot be taken off in the office like the jacket.

For evening wear in the hot weather a *kamarband* is unnecessary. A black alpaca jacket is the lightest and in the long run the cheapest garment.

A monocle lessens the burden of glasses and can be carried with ease and worn with dignity with very little practice. Glasses (2 pairs) can be left in the office and in the study.

For those who will benefit particularly by the suggestion in dress, because of their state of nourishment, one suggestion in refreshment is also offered: solid food must be reduced and may be replaced by liquids if necessary. Even beverages that cheer a little more than tea, coffee or milkshakes, will take a long time to damage the body, if they do any damage at all. But a heavy meal specially when one is dressed in tight clothes can incapacitate, distress or kill the consumer at one sitting. The contents of the abdomen prevented from expanding outwards by tight clothes push the diaphragm upwards and embarrass the heart. Later, during the night, extra demand on circulation made by the digestion can produce myocardial ischaemia and heart failure. That is how so many important business and literary men die after banquets. It is a pity that sociability has become associated with feeding, by custom. Beverages with the lightest of solids should replace this feeding, as a rule, in middle age.

For footwear well-fitting *chaplis* are ideal for the day in summer. They have beaten many an enemy in many a battle-field.

S. D. S. G.

FEEDING THE WORKER

THE factory canteen forms an integral part of modern large-scale industry, as it contributes much to the well-being and efficiency of the worker. In Britain, during the war, such canteens multiplied with the growth of various industries, and side by side there arose hundreds of British restaurants for the convenience of many people who were obliged by circumstances to take their principal meals elsewhere than at

home. These establishments became very popular as they provided workers with satisfying and balanced meals at moderate charges, and it may be said that they were among the factors that contributed to the health of the nation in war time. In India, too, canteens have been set up in several factories where employers have come to realize that a well-fed and contented worker is a valuable asset, but they have not developed to the extent one would wish and only a few of them exist, so far as we know, for non-industrial people. In view, however, of shortage of food all over the world, it is most desirable that collective feeding should widely extend its range and give a chance to workers who do not get sufficient food to keep them going under the strain of modern life.

A good canteen should be a place where wholesome and inexpensive food can be had in cheerful surroundings. By purchasing foods from the rationing authorities and catering on a large scale, the costs can be kept down to a low level. Management may be in the hands of the factory itself or an outside firm, but it is desirable that the managers should know the nutritional value of the food which they purvey. They must also know how best to prepare food, how to prevent or reduce wastage and how to present a variety of dishes. The British restaurants aimed in supplying in one meal a third of the day's requirements of proteins and calories, and two-thirds of the vitamins and mineral salts; perhaps it will not be difficult for our canteens to adopt a similar standard. But in times of scarcity calories come first, and protein, vitamins and mineral salts must assume a secondary rôle.

To show what can be done with existing resources, we might give a few details of the 'square meal' canteen which has been started by the Bombay Government to provide employees of its Secretariat and the allied offices with a substantial well-balanced meal at a cost not exceeding six annas (*Feeding the Worker*, January 1946. Government of India). It is a large and pleasant place situated close to the offices and is very well equipped. It consists of a common room, a spacious dining room, pantry, kitchen and scullery, and a store-room. The dining room has two halls furnished with tables and chairs which can seat 210 persons comfortably and which are fitted with electric lights and fans. The walls are painted cream with a view to absorb the glare of the sun. The kitchen is amply provided with all the necessary utensils, and the store-room is fly- and rat-proof and lined with glaze tiles. The menu is purely of vegetarian items and comprises chapatties, rice, dhal, two vegetables, vegetable salad or pickles, butter-milk and chutney. A maximum of eight chapatties is served to each customer, and the quantity of rice is 2 ounces; occasionally sweets are also served. The canteen is run entirely by the government staff with the help of an advisory committee which

includes two ladies and the nutrition officer of the government. The canteen is well patronized and no communal or caste distinctions are observed. The meal at the 'square meal' is in addition to the rationed foods to which an individual is entitled.

The food can, of course, be varied to suit different requirements. Such canteens are of immense value to those classes of people who are unable to supplement their meals with extra food. Dietetically they have also an educative value. Their controlled charges, reliable meals and general convenience, once appreciated, will carry them as going concerns even in normal times. We understand that the Government of India is taking action to set up restaurants, at first to be confined to the large cities, with the idea of supplying wholesome meals at a price that the average man or woman can afford. There are difficulties, of course, as getting of suitable premises, but there has never been a more favourable opportunity than the present of putting into operation community feeding which is part of the daily life in our army and which can be spread among the civilian workers with equally beneficial results.

R. N. C.

Special Article

TRANSMISSION OF KALA-AZAR IN INDIA: THE CASE AGAINST THE SANDFLY—A REPLY *

By H. E. SHORTT, M.D., D.Sc.

COLONEL, I.M.S. (Retd.)

WHEN the paper by Malone and Brooks (1944) was first brought to my notice, I felt some difficulty in taking it as a serious contribution to literature in connection with the problem of transmission of kala-azar. I was strengthened in this opinion by my personal knowledge of both authors, more especially of one of them, whom I know to be a very fervent admirer of Mr. Bernard Shaw, and I came to the conclusion that the whole article was written in the shavian tradition, with the authors' tongues in their cheeks and with the intention of raising a controversy about a subject on which the authors hold no serious views. As I have seen no reply in the medical literature to the arguments

* By a coincidence a letter from Colonel Malone on the subject has also been received. It appears on page 333.

brought forward in the paper it may be said that this object, if I am correct in attributing it to them, has failed. I thought it right, therefore, after a lapse of over a year, to make some reply to the theoretical objections raised by the authors against the generally accepted view that transmission of kala-azar is effected by the bite of the sandfly, in order to prevent those unfamiliar with the original work which is discussed in the paper from being misled by the specious and superficially plausible arguments brought forward.

I have no desire to deal with every point raised by the authors of the paper, a procedure which would be tedious and unnecessary, for it can be shown that the more important deductions arrived at by them are incorrect. The simplest way in which to proceed with this task would appear to be to take the various statements made which the present writer considers incorrect and to show wherein Malone and Brooks have erred, either in presentation of facts or in their interpretations of these.

The paper, after an opening section, is divided up under a series of headings and these will be dealt with *seriatim* under the same headings.

The opening paragraph of the paper contains two mis-statements which are an early indication of a lack of care in reading the literature from which the deductions of the paper have been drawn. The statement is made: 'Their efforts appeared to be crowned with success when Knowles announced infection by flagellate forms of *L. donovani* extending into the buccal cavity of *P. argentipes*, and it was considered that the case for the sandfly had been proved except for demonstration of the actual transmission of the disease to human volunteers'. So far as I know Knowles never made any such announcement and the description of infection of the buccal cavity of *P. argentipes* with *L. donovani* was first given by Shortt, Barraud and Craighead (1926).

The second mis-statement in the opening paragraph was to the effect that Swaminath, Shortt and Anderson (1942) reported successful transmission of kala-azar by the bites of experimentally infected *P. argentipes* in every one of seven volunteers bitten. In fact, the report was on five volunteers only. As this report was presumably the precipitating cause of their attack on the sandfly theory of transmission it is a pity that they betray by this inaccuracy the casual manner of their reading of the work of others, especially as their theoretical deductions are based entirely on published work, and not on any original investigations. They go on to say that: 'Successful transmission of the disease has been achieved by a special technique of breeding and feeding *P. argentipes* in the laboratory by means of which the duration of life of the flies has been prolonged to ten days or longer, thus permitting the flagellate forms to develop fully; the flies have been induced to take more than one blood meal, and they have been "blocked"

as a result of an artificial diet of raisins'. It may be pointed out that Shortt, Barraud and Craighead (1926) described this 'blocking' of flies long before the technique of feeding on raisins had been brought into use and pointed out the probable importance of this condition in its relation to transmission of kala-azar.

After these initial false starts the authors of the paper proceed to discuss published evidence of transmission by the bite of the sandfly under certain headings which will now be considered in a similar manner.

BIONOMICS OF *P. argentipes*

(a) *Duration of life and feeding habits in nature and in the laboratory*

With regard to the question of the length of life of the sandflies in nature the authors refer to experiments carried out by Smith *et al.* (1936) where flies marked by various means were released and subsequently searched for in the same area. Commenting on this work they say, 'If then (after a reliable method of identification had been introduced), not a single fly out of 3,271 plus 428 could be recaptured by these experts after the sixth day and the flies did not migrate, it seems fair to conclude that *P. argentipes* in natural surroundings does not normally live longer than six days.

'This is in large measure confirmed by the earlier work of Christophers which showed that female sandflies, bred in the laboratory or caught in nature and kept under the most natural and favourable conditions possible, invariably died immediately after ovipositing (Christophers *et al.*, 1926, 1926a)'. In their comments it has suited the authors to ignore the previous experiment of Smith *et al.* where, out of a much smaller number of flies (667) released, recoveries of marked flies were made up to the fifteenth day. Our knowledge of the physiology of the sandfly makes it certain that such flies must have fed a minimum of three times to live for so long a period. They go on to criticize admittedly unnatural methods of prolonging the life of the fly after oviposition, such as the segregation of the sexes to prevent fertilization and oviposition. They do not say, however, that procedures such as this were temporary expedients when less was known about the bionomics of the fly, and which were discontinued as soon as more natural methods of prolonging the life of the fly were substituted, as a result of study of the conditions under which the fly lived in nature.

They also criticize the technique whereby the flies were kept at a continuous temperature of 28°C. with a variation, plus or minus, of not more than 2°C.; they remark in this connection that the 'Official records show that the average temperatures recorded at Dibrugarh, Sibsagar, Tezpur, Gauhati, Dhubri, Silchar and Srimangal in Assam were fairly uniformly 30°C. throughout the months of May to August, and that the

daily variations were always greater than 5°C. at any of these places—a variation too great for laboratory-kept flies to withstand'. These meteorological figures presumably refer to data taken in the ordinary way and would represent the figures in the open. The sandflies themselves are normally found inside houses, or cattle sheds, where the conditions are considerably modified with respect to those obtaining in the open; they are still further modified in the cracks and crannies in which the sandflies habitually hide when not out looking for food. Such situations are not subject to any extent to movements of air which would cause evaporation of moisture and subsequent cooling. The conditions in these cracks are of fairly uniform temperature throughout the day and night in the monsoon period, and correspond closely to the conditions artificially reproduced by us in incubators. In fact the latter were a deliberate attempt to reproduce as accurately as possible the conditions found prevailing in nature and could not justifiably be called unnatural and far removed from the environment of flies in nature. In quoting the opinion given by Shortt *et al.* (1932) that in performing the act of fertilization the males die, having paid their full debt to nature, they go on to say 'It is probable that in ovipositing the female also pays her full debt to nature'. In other words they imply that the female is intended to lay eggs once and then die. If the authors had even a slight knowledge of the anatomy of the female sandfly they would know that each possessed an organ called a spermatheca, which on the act of fertilization, soon after the emergence of the fly, collects in it a large store of spermatozoa intended to fertilize future batches of eggs. Were the sandfly intended to lay only one batch surely nature would not have gone to the trouble of supplying it with a special organ for the storage of spermatozoa which would never be used. Apart from all other arguments brought forward and which there is no space to consider individually, this one fact would seem completely to demolish the structure of their argument.

We are unaware why the writers take such exception to the feeding of sandflies on raisins and infer that this should nullify the results obtained thereby, *viz.* the production of successful transmissions to man by the bites of flies so fed. In keeping mosquitoes for experimental work these methods of feeding on raisins or other plant juices is a normal procedure, but nobody has inferred from this that the mosquito would normally prefer plant juices to blood as its diet, and there seems no reason to suppose in the case of the sandfly any more than in that of the mosquito, that the normal food may not be blood, simply because the insect can be made to feed on plant juices. That the latter are not the normal food is further evidenced by the fact that the ovaries of the fly will not develop except after a blood meal. This has been shown in the case of flies which have been fed on plant

juices from the beginning, and also in those fed on plant juices in feeds subsequent to the first blood meal. A little more knowledge of the bionomics of insects in general, to say nothing of *P. argentipes* in particular, would have deterred the authors from developing this argument.

(b) *Flagellate infections in the laboratory*

In the last paragraph of this section the writers, in talking about 'blocked' flies, apparently take it for granted that flies in nature definitely do not feed on plant juices, and also, that unless they did so they could not become 'blocked', as would appear from the following quotation: 'And we consider it highly improbable that such a condition could happen in nature where flies do not feed on raisins, and do not live long enough for "blocking" to occur'. I see no reason for either of these assumptions. In the first place, it would be difficult to prove that flies never feed on plant juices under natural conditions, and in the second place, such food is not at all necessary in the production of the condition known as 'blocking'. This condition was originally described by the present writer and his collaborators in 1926, where the actual condition of 'blocking' was described for the first time, and its similarity to the condition found in plague fleas pointed out.

(c) *Flagellate infections in nature*

At the beginning of this section the writers say that the condition of massive infection of the buccal cavity of *P. argentipes* is only found in flies kept under rigidly maintained artificial conditions, and that in twenty years of unrelenting research, not a single *P. argentipes* has ever been recorded with a natural infection of *L. donovani* extending to the pharynx or beyond. The fallacies in this argument are only too obvious. In the first place, the search for *P. argentipes* infected in nature was by no means unrelenting during twenty years, and in fact was only occasionally pursued; in all, the number found infected in nature could probably be counted on the fingers of both hands. In the case of flies bred and fed in the laboratory, the number reaching the condition in which flagellates were contained in the pharynx was a comparatively small proportion of those actually infected, although the latter must have numbered many thousands. It is not surprising, therefore, that no case of infection of the pharynx was found in any of the few infected flies caught in nature. They go on to say that the report by Shortt and his collaborators (1930) on seven infected flies out of 226 examined, may lead to the assumption that about 3 per cent of *P. argentipes* in kala-azar areas are naturally infected. I do not know who makes this assumption, but it was certainly not made by the Kala-azar Commission. They further state that six out of the seven flies were not caught,

as stated by Wenyon (1932) from kala-azar houses, but in a cattleshed. Apart from this being an incorrect statement—Wenyon is correct—they again display ignorance of local conditions in Assamese houses. The cattleshed, as often as not, forms part of the house itself, and is normally always immediately adjoining it. It would be as easy, therefore, for the sandflies after feeding to come to rest in the animal as in the human part of the house.

(d) *Other biological considerations*

At the beginning of this section, the writers maintain, with regard to kala-azar, that it is a disease of the reticulo-endothelial system, and of the skin, and cannot be regarded as a disease of the blood stream. They further go on to say that in kala-azar parasites may occasionally be found free in the blood stream, but for the most part within the leucocytes, and in particular in the large reticulo-endothelial cells. They state: 'The presence of the parasite in the blood stream then can only be regarded as an accident for the parasite rather than a biological necessity'. It is difficult to understand why these assumptions should be drawn, when it is a fact that the parasite in Indian kala-azar can be found in the blood in over 80 per cent of cases by direct microscopical examination (Shortt *et al.*, 1927) and in practically 100 per cent of cases if cultural methods are used (Das Gupta, 1923). The fact that the parasites in the blood are usually not free, but within elements of the reticulo-endothelial system, is only natural, since that is their natural habitat.

In the next paragraph protozoologists are accused of taking it for granted that an insect vector must be involved in the transmission of kala-azar. The writers then say: 'No parasite having the life cycle of *L. donovani* is transmitted in any way other than by a biting insect. This is so generally true that it would outweigh any evidence to the contrary were it not for certain unique differences which kala-azar exhibits when compared with insect-borne diseases'. The meaning of this paragraph is not quite obvious, but they go on to say that the assumption of an insect vector may be wrong as shown by the following facts:—

(a) 'In diseases transmitted by an insect vector, infection can be experimentally transmitted only by the bite of the infected insect (or its laboratory equivalent, inoculation). Malaria, trypanosomiasis, yellow fever, relapsing fever, typhus, bubonic plague, all illustrate this. But Shortt *et al.* (1932) have shown that kala-azar may be experimentally transmitted with comparative ease to Chinese hamsters by ingestion and proximity'.

My only comment on this is that I have also been able to demonstrate that malaria, both in birds and monkeys, can similarly be transmitted by ingestion, and this observation has been verified independently. The same facts apply

to infections with various trypanosomes. This argument therefore falls to the ground.

(b) 'In such diseases, the parasite is in the blood stream; in kala-azar, it is more probably in the skin'.

I cannot see in what way this statement could strengthen the case of the authors against an insect vector and, in any case, it is demonstrably misleading.

I have already stated that the parasite occurs in practically all cases of Indian kala-azar in the blood stream. Its presence in the skin would appear to facilitate, rather than otherwise, transmission by a blood-sucking insect, and it has been shown by the present author and his collaborators that *P. argentipes* fed on skin lesions becomes infected (Shortt *et al.*, 1928).

The writers then attempt to strengthen the case against the sandfly on the grounds that kala-azar is not found in all areas where *Phlebotomus argentipes* exists. This argument is difficult to follow, because *P. argentipes* could only become infected and act as a vector in an area where cases of kala-azar were present. The fact that *P. argentipes* is found in Ceylon and in Bombay and does not there transmit kala-azar is sufficiently explained by the fact that kala-azar is practically non-existent in these areas. The same argument might have been used in the case of Assam before that province had cases of kala-azar imported and so became the scene of the most spectacular outbreaks of this disease. A similar state of affairs might be said to exist in Great Britain where there is practically no indigenous malaria, although anopheline carriers of malaria are abundant in many areas. That these carriers are fully efficient is proved by the previous existence of malaria in Great Britain in areas such as the Fens and by the occurrence of sporadic outbreaks after the war of 1914–18, when the mosquitoes became infected by feeding on cases of malaria which had come from other countries and supplied a source of infection for the indigenous anophelines. The next point made by the writers is that flagellation in the sandfly is not necessarily of biological significance, since a similar flagellation occurs in the bed-bug, and they make the statement: 'Anterior development in the sandfly, as we have seen, only takes place when the life of the fly is artificially prolonged'. This is a simple mis-statement of fact and is not correct, since anterior development occurs even after the first feed of the sandfly. They go on to say, 'The fact that flagellates of a water scorpion can give rise to leishmania-like infection in mice, a parasite and host that would never come together in nature, induces a complexity to the problem'. The experiments which form the basis for this statement may be said now to be completely discredited, a fact which a little further reading on the part of the writers would have made clear to them.

(e) *Epidemiological factors*

1. Under this heading the statement is immediately made, 'it is generally assumed that the distribution of kala-azar coincides with that of *P. argentipes* in India'. The present writer is not aware by whom this assumption is made and it would be more accurate to say that the distribution of *P. argentipes* includes all areas in India where kala-azar is found. The probable reason why the distribution of one is greater than that of the other has already been touched upon. The next piece of so-called evidence to be brought forward against the sandfly hypothesis is the fact that, in Madras, Patton stated that the number of sandflies is very limited, the only species being *P. minutus*. The fact that the Kala-azar Commission later proved the presence of *P. argentipes* in the great majority of houses in the very part of the town referred to by Patton is brushed aside on the assumption that *P. argentipes* had only recently reached Madras, and that cases of the disease previously known to occur must have been produced by means other than the sandfly. This sudden extension of the range of *P. argentipes* is not explained by them! The remarks on a few cases occurring in Sanawar in the Himalayas hardly call for answer, because the facts about them were never sufficiently cleared up, and it is most probable that the cases did not acquire their disease locally, but actually came to Sanawar already infected in another part of India. They maintain from the history of these cases and from some of the writings of Rogers (1914), Korke (1913) and Michael (1926) that the probable method of infection is close contact with a previous case. In this respect they conveniently ignore the fact that, in the areas dealt with by these writers, *Phlebotomus argentipes* is common and that there is every chance of its becoming infected from the case or cases with which people are in contact, and so passing on the infection to the latter. This section is closed by the following statement: 'Further, the observations of two eminent entomologists carried out during many years, Patton's in Madras and Sinton's in Sanawar, suggest that kala-azar can be present in the absence of *P. argentipes*'. This statement is not supported by facts, and so far as I know the presence of *P. argentipes* has been demonstrated in every area in India where undoubted indigenous cases of kala-azar have occurred.

2. *Age incidence*.—As is well known in Indian kala-azar the disease may occur at any age, but is most common in children and young adults, being much more uncommon in infants. This is put forward as evidence against the theory of transmission by a biting insect. We are not prepared to argue on this point as many factors are involved, but it might be pointed out that in the Mediterranean area kala-azar is essentially a disease of infants. The fact that this latter age incidence would not support their

theory along the lines of the argument developed by them seems to have been ignored in their paper.

3. *Sex and race incidence*.—The evidence under these headings is too indefinite and involved and I do not propose to say anything under this heading.

After considering the last two sections they ask a series of questions:—

'How does the sandfly transmission theory account for the following epidemiological observations'?

1. 'The disease is rural rather than urban':

The same might be said of malaria and it may be pointed out that the neighbourhood of houses in rural areas provides ideal conditions for the breeding of sandflies. Had the authors of the paper spent as much time as the present writer in looking for breeding places of sandflies they would have realized that suitable conditions can be found easily both in cities and in rural areas and that some other reason for a greater prevalence in rural areas must be sought.

2. 'Old' coolies ('old' by length of residence not in years) are more susceptible than newcomers.

That this should be so, for it is indeed a fact, is only natural in the case of a disease where a small percentage of vectors reach the stage for transmitting the disease, and where the incubation period may be a prolonged one. This would mean that the longer an individual remained in a danger area for transmission, the more likely he would be to acquire the disease.

3. The failure of the disease to spread in Ceylon has already been dealt with.

4. 'The failure of the disease to spread in schools and hospitals, although it is a house infection'.

It is not at all certain that the disease does not spread in such institutions, but possibly the long incubation period would mean that in the case of hospitals, at least, many of the patients would have left the latter before showing symptoms of an infection.

Geographical distribution

There is nothing in this section calling for special comment, although not everyone would agree with all of the statements made in it.

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Medical News

WARTIME INVENTION HELPS DEAF CHILDREN

By MARY EVANS-JONES

(Reprinted from Release No. MNL/105 offered by the Public Relations Officer, Australian High Commissioner's Office, New Delhi.)

UNABLE to hear any sound until six months ago, a small group of four- and five-year-old children now attend lessons at a kindergarten in Sydney, Australia, where experiments in teaching them to hear and speak may have far-reaching results for hundreds of other children similarly affected.

Wide interest is being shown in the efforts of physicist-engineer N. E. Murray and his team of 10 laboratory workers and psychologists. Using experience gained during the war in perfecting inter-communications for the Army and the Royal Australian Air Force, for servicemen suffering from masking deafness, and for temporary deafness induced by the roar of planes, tanks and guns, Mr. Murray has developed a powerful hearing aid for the children.

Further development of the 'walkie-talkie' aid, he says, may greatly relieve 90 per cent of the children whose deafness has resulted from German-measles (Rubella) and 50 per cent of those deaf from other causes.

He also hopes that when new devices are perfected and easily obtainable, children now confined to institutions may be able to come out and take their place in the world.

Hundreds of children were born deaf in 1940-41 because their mothers, during pregnancy, had suffered from German-measles during an epidemic. Young

women were the principal sufferers. In many cases, it was not until the children were almost a year old that the parents realized something was wrong. The children were making no effort to talk. Gradually the grim legacy of the epidemic was revealed. The 400 Rubella deaf children, as they are called, had almost doubled the number of deaf and dumb children in Australia.

Some of the children most gravely affected were born with weak hearts, partial or complete blindness, or damage to internal organs. But in most cases only their hearing had suffered; in every other way they were normally healthy. As in most cases of congenital deafness, muteness or partial muteness is secondary; they are not dumb because their power of speech is affected, but because they have never been able to hear.

Appeal to science

Parents who had no reason to suspect that their children might be deaf because of family history appealed to the Acoustic Research Laboratory, National Health and Medical Research Council, a department of the Commonwealth Department of Health. Their pleas for help went to the officer in charge, Mr. N. E. Murray, a physicist-engineer, who had returned from northern battle areas at the end of 1944 and was giving his full attention to civilian needs.

He recognized the similarity between the deafness of servicemen and the children as a so-called nerve deafness, and immediately went to work on the problem of measuring the extent of hearing loss. The standard method was to measure the loss at certain defined frequencies or pitch over the voice range, so that a good indication of the loss of hearing, or deafness to speech, could be obtained. This had been comparatively easy with servicemen who, not having always been deaf and therefore able to talk, could readily indicate the point at which they could just hear. The problem was to devise some method of making it possible for a deaf child to give a similar indication that it had heard a sound.

Mr. Murray reasoned that if animals could be trained to give a condition response, he saw no reason why young humans could not be trained likewise. If a dog could become so accustomed to receiving its food when a bell was rung that its mouth would water at the ringing of the bell, why not try a similar method with children?

By careful conditioning, a suitable reaction was produced with children of 3½ years. First they were taught by sign association to give a conditioned response, such as placing a coloured counter in a box, or to make a mark with a crayon when a very strong whistle was blown close beside them. They first learned by the sight of the whistle being blown, rather than by the sound, which they could barely hear; later learned to place the counter in the box on hearing the faint sound.

By this association, it was possible to measure by an audiometer the point where they just began to hear. The audiometer is the standard instrument used for measuring hearing loss, commonly used by hearing aid dispensers. Mr. Murray designed a special instrument to measure more than ordinary hearing loss. It was first turned to a volume where the child could hear with the aid of an earphone. It was next brought down very low, so that the child could not hear at all, and then brought up gradually louder, until the child, at the first noise it caught, would place a counter in the box. This was usually at a volume and pitch which would sound quite loud to normal ears, but which was just audible to the child.

By discovering the child's reaction to varying volumes and pitches of sound, it was possible to complete audiograms from which hearing aids might be most efficiently designed, and therefore most effectively provide sound to train the children's speech.

Portable aids

The first hearing aid designed for the children by Mr. Murray was a group aid, with 10 separate outlets,

*These references have been included in the Editor's office. Although occurring in the text, they were not supplied by the author.—EDITOR, I.M.G.

each individually adjusted to the children's own audiograms. Portable aids of an individual kind are now being introduced, adjusted to the needs of the individual children. The first three aids of this type were tried for the first time in April 1946.

Portable aids have two great advantages: deaf children need not be grouped together for their lessons, but may sit in a class-room with normal children, and the microphone, instead of being in the centre of the table, is concealed in the headset.

Generally one ear is found to be worse than the other, so the good ear is used for the output of the amplifier. Mounted on the headset in position of the other ear is a microphone, in the same shape as the other earphone. This gives a much more effective mounting of the microphone than any other, as it simulates the sound waves reaching the ear. Operated by batteries, portable aids last for months without needing to be re-charged. Later this year it is hoped to provide individual aids for each child who has reachable hearing.

The two main advancements made by Mr. Murray and his team of ten laboratory workers and psychologists are, in his opinion, the establishment of contact with deaf children at a particularly early age, and the fact that those handicapped are mixing and becoming normally adjusted to normal children, and leading a natural family life. They attend nursery or primary schools with normal children, attending their special classes with the group hearing aid two days a week.

The co-operation of the government-subsidized Kindergarten Union and the Department of Education has made it possible for the Rubella deaf children to attend school with other children. Naturally, they need more individual attention than their playmates, but it is surprising how well they respond to trained Kindergarten teachers, and learn to follow the example of normal children around them.

Mr. Murray says he will never forget their smiles when they were first introduced to the group hearing aid, and heard for the first time. 'It made you feel you wanted to lock yourself up away from everyone else, and work 24 hours a day to do everything for them as quickly as possible', he said.

As treatment is considered to be still in the experimental stage, no charge is made to parents for any of the equipment used, or for tuition. The portable individual hearing aids now being used are to be replaced by 'walkie-talkie' attachments which may be worn on the children's backs, so that they can move about freely. Manufacture of this type of aid is dependent on the importation of components not made in Australia, such as 10-millimetre tubes, special small earphones and crystal microphones.

FLEMING: DISCOVERER OF PENICILLIN

(Abstracted from a Circular dated 26th May, 1946, issued by the Press Information Bureau, Government of India, New Delhi.)

On a morning of September 1928, Alexander Fleming, teacher of bacteriology in St. Mary's Hospital Medical School, happened to lift the lid off a dish in which he was growing a bacterial culture. A casual mould-growing spore fell into the dish before the lid was replaced.

A few days later Fleming saw that a greenish-blue mould was growing on the surface of his bacterial 'garden'. As a culture it was ruined. It was no new thing for a mould to ruin a bacterial culture. Normally the whole thing would be thrown away. But this mould was different, for Fleming saw that it had cleared the bacteria from quite a wide area. Here was a substance of some importance as a destroyer of dangerous bacteria. The dish was *not* thrown away. The green mould produced drops of yellow liquid which, even when diluted 800 times, prevented the growth of dangerous staphylococci. Under a microscope the mould was made up of tiny particles shaped like a pencil. He called it penicillin.

In 1938 Dr. Florey, an Oxford professor, and a small team of experts, began a series of experiments which turned this green mould into a powerful instrument of healing, which saved not only hundreds of lives on the battlefield, but rescued as many shattered limbs from the surgeon's table.

Alexander Fleming, who made all this possible, was born in 1881, the son of a Scottish farmer. A brilliant schoolboy, whose early career was a record of scholarships and gold medals, he eventually became a teacher at London University. There he was assistant to Sir Almroth Wright, the father of modern vaccine therapy. At his side, he contributed to the research which produced World War II's first wonder drug, M.&B. 693, and he it was who discovered that tears contain an antiseptic substance called lysozyme, a discovery of great physiological importance.

Like all great scientists Fleming's work was motivated by a great humanitarian perception as well as scientific curiosity. It was his work as an Army doctor in World War I that set him thinking on the lines that eventually led him to his great discovery. For all around him he saw the ravages of invisible bacteria robbing men of life and limb. He made bacteriology his special study. His brilliant work, crowned by his discovery of penicillin, has marked him for lasting fame.

In 1944 he was knighted for his great services to science and the cause of humanity, and in 1945 he received (jointly with Florey and Chain who had extracted penicillin for therapeutic use) the Nobel Prize for Medicine. Academic honours showered on him. He was awarded the Legion of Honour by the French people and was made not only a member of the Academies of Medicine in Paris and Rome, but a member of Britain's Medical Research Council.

THE BRITISH INSTITUTE OF PHILOSOPHY

(Incorporated under the Companies Acts, 1908-1917, as a Company not for profit, but limited by Guarantee)

ON the 6th of April this year the British Institute of Philosophy has come of age. Founded under the late Lord Balfour, its purposes are to serve as a link between philosophers and the everyday world, and to spread such general understanding as can be reached of the universe in which we live and of man's place in it. Its council has been throughout composed of leading representatives, not only of philosophy, but also of science, of politics, and of industry and commerce. The present president is The Rt. Hon. Viscount Samuel, G.C.B., G.B.E., M.A., Hon. D.C.L., chairman of council Sir W. David Ross, K.B.E., Litt.D., LL.D., F.B.A., deputy chairman of council The Rt. Hon. Lord Lindsay, C.B.E., M.A., LL.D., director of studies Sydney E. Hooper, M.A., and hon. secretary P. M. Rosedale, LL.M. Local branches have been formed in several cities. *Philosophy*, the quarterly journal of the institute, contains articles by writers of distinction on the great philosophical questions as well as reviews by specialists of the important new books on such subjects published in the United Kingdom or other countries. The membership exceeds a thousand. The annual subscription is only one guinea, which includes receipt of the journal, and there is no entrance fee. The council appeals to those interested to join the institute. Application for information and forms of membership should be made to: The Director of Studies, The British Institute of Philosophy, University Hall, 14, Gordon Square, London, W.C.1.

DIET SURVEY IN COLLEGE AND SCHOOL HOSTELS IN DELHI*

IN this survey, the diets of two large groups of boys and girls in hostels in Delhi were studied—one consisting of well-to-do college students and the other of school children who came from very poor families. Wheat was the main item in the diet of both groups,

and the calorie intake ranged from 2,142 to 2,693 in school children and 2,447 to 3,935 in college students. The report* says that the total protein consumption appeared to be satisfactory, but the proportion of animal protein left something to be desired. One remarkable fact disclosed was the habit of taking very small amount of leafy vegetables which could form a good source of pro-vitamin A and as vegetable fat was used in these institutions, milk and ghee being costly and scarce, the diet was short of standard vitamin A requirements. Vitamin B₁ and B₂ content could be taken as adequate, as the diets were based on whole wheat and pulses, which are quite good sources of B₁ and most members of B₂ group. In some institutions salads consisting of onions, green chillies, tomatoes, etc., with or without lime juice were taken. These provide a good source of vitamin C. With some exceptions the diets were inadequate in respect of fruits. While the college students took reasonable amounts of milk and milk products, the school children had very little of them. The intake of fat and calcium in the case of the latter was also below normal. Out of 391 children examined, 7 showed the presence of Bitot's spots. No other deficiency disease was found. The author recommends the use of skimmed or butter-milk where whole milk is unobtainable and of adequate quantities of leafy vegetables, and inclusion of some uncooked green vegetables and fruits such as mangoes, papaya, tomatoes and oranges.

* Diet Survey in College and School Hostels in Delhi. By Dr. K. L. Shourie, B.Sc., M.B., B.S. (Punjab), M.Sc. (Madras), M.D.S. Special Report of the Indian Research Fund Association, No. 14. Published by the Indian Research Fund Association, New Delhi. Pp. 16 with 5 diagrams. Price, Re. 1.

TYPHOID ENDOTOXOID IMMUNIZATION

Prior to 1934, the incidence of typhoid fever among the native labourers in the Transvaal gold mines was high, owing to their insanitary habits and presence of large numbers of 'carriers' excreting typhoid bacilli. In that year, it was decided to give a large-scale trial to the new type of typhoid endotoxoid vaccine, and with it there was a dramatic fall in both typhoid incidence and mortality rates which has continued during the subsequent years of systematic immunization. The vaccine contains, in a soluble atoxic form, the antigenic principles of *B. typhosus*, *B. paratyphosus* A, B and C. The reactions following the inoculation of two doses of 0.5 and 1 c.cm. are very mild, and this has made mass inoculation possible. The statistical results of ten years' work are reviewed by Dr. E. Grasset in a recent publication issued by the South African Institute for Medical Research.

INFANT WELFARE IN AUSTRALIA

(Abstracted from Release No. MNL/104 offered by the Public Relations Officer, Australian High Commissioner's Office, New Delhi.)

In a most interesting and informative way the author Dr. Ella Sandford Morgan refers to the progressive development of infant welfare services in Australia. Dr. Morgan has made a very commendable attempt to place before the readers a systematic study of the movement in the Southern Hemisphere. Her historical introduction of the work from 1904 gives a complete picture of the welfare services, the steady and gradual fall of mortality rates. Australia is now proud of her infant welfare system and having the lowest infant death rate in the world. Much of the reduction in the infant death rate, Dr. Morgan described, is due to the excellent infant welfare services and a wave of social betterment spread over the country, with higher wages, better living conditions and improvement in sanitation, water supply and general health services.

Although the principles followed are fundamentally the same the infant welfare centres in Australia

differ from centres in the other countries in certain respects—as no treatment is given in the centre, the breast nursing of infants to at least 9 months is insisted upon. Australian centres do not have orthopaedic clinics, dental clinics, etc., attached to the welfare centre. There are some interesting methods of services carried out such as Baby Health Cars, conducting clinics by travelling by planes from the railhead to a remote corner of the State, a motor caravan and motor cars provided another type of service. Still more inaccessible places are served by a comprehensive correspondence system. Australian health personnel, it is stated, received high standard of post-graduate training and the services rendered by them is uniform. Australian babies receive care and supervision second to none in the world.

A. B.

FREE NATIONAL MEDICAL AID PROPOSED*

(Reprinted from Release No. MNL/106 offered by the Public Relations Officer, Australian High Commissioner's Office, New Delhi.)

A COMMITTEE of State and Federal representatives will investigate Commonwealth Government plans for a free national medical service. This was decided at a conference of State Health Ministers and the Federal Minister for Health, Senator Fraser, in Canberra. The conference favoured the proposals put forward by Senator Fraser, but decided that their practicability should be investigated. The investigating committee will consist of State-nominated officers and three Federal representatives.

The Commonwealth proposals were:—(1) Every person in Australia, without regard to his or her economic status, shall be entitled to free medical attention, including diagnosis and treatment. (2) The Federal Government shall establish and maintain medical centres wherever needed in city and country areas. (3) Flying doctors and mobile medical units shall be employed in remote areas. (4) Training schools for pathologists, biochemists, radiologists, technicians, and other specialists shall be established.

The conference decided that the committee should, if it thought desirable, recommend that State Governments act on behalf of the Commonwealth in administering the scheme. It also decided that the Commonwealth should legislate to introduce the scheme, but only if additional social services powers to be sought by referendum later in the year were granted. Outlining the Commonwealth proposals, Senator Fraser said: 'The Commonwealth will not sponsor any half-baked plan. The Commonwealth intends that whatever scheme is introduced shall be complete'.

Doctors now in practice would be given the opportunity to join in the service on either full-time or part-time salaried basis. Doctors and patients would be free to make private arrangements outside the service.

B.M.A. plans Medical Benefits Fund

A benefit fund is planned by the British Medical Association in Australia, under which adult contributors, for a weekly payment of Re. -/13/-, will have to pay only Rs. 1/9/8 for every ordinary visit to a doctor. The fund will be controlled by a separate non-profit-making organization registered under the Companies Act. The Secretary of the B.M.A., Dr. Hunter, said that the plan was not intended to forestall introduction of a government-controlled free doctor service, but would provide people with an easy way of paying heavy medical expenses. Proposed contributions are Re. -/8/6 a week for persons under 21, annas 13 for persons between 21 and 60, and Rs. 1/9/8 for a family group without children under 17. Contributors will

* This is in conformity with the proposed establishment of a new health service in England and with the recommendations of the Bhore Committee for India.—EDITOR, I.M.G.

benefit by Rs. 4/- for every visit to a general practitioner, by Rs. 11/3/10 for the first visit to a specialist, and by Rs. 5/10/- for each subsequent visit. A yearly limit of Rs. 161/2/- is set on the benefits. For major operations, contributors will benefit by Rs. 280/-.

The Commonwealth Government would welcome B.M.A. co-operation in planning a free medical service for the people of Australia, said Senator Fraser when he heard of the B.M.A. scheme. 'I have not closed the door to the B.M.A.', he added. 'I made it clear to the B.M.A. some time ago that the Commonwealth proposed introducing a scheme under which medical services would be provided for the people without direct charge. I asked the B.M.A.'s help in planning the service, and I am still prepared to confer with the Association on this matter. I have never ignored suggestions made by the B.M.A.'. Asked whether he thought the B.M.A. scheme was designed to forestall the Government scheme, Senator Fraser said: 'You can draw your own conclusions'.

Aluminium treatment for miners' complaint

Keen hopes are held for the prevention of silicosis, by the aluminium dust inhalation treatment, and the arrest of development of the disease in established cases. Encouraging results have accompanied research into the subject, particularly in Canada and the U.S.A. Dr. W. E. George, of the Bureau of Medical Inspection, Broken Hill, New South Wales, is at present visiting North America to investigate the status of 'aluminium therapy' there, and to discuss clinical aspects with medical officers associated with the research, government departments, and sufferers from the complaint who have been undergoing treatment for several years. His visit is sponsored by the Department of Post-War Reconstruction, with the concurrence of the N.S.W. Government through the bureau to which he is attached. Indicating the keen interest which the Australian Institute of Mining and Metallurgy is taking in the question, the Institute strongly supported sending Dr. George abroad, and as part of its activities in the last year published a booklet entitled 'Aluminium Therapy In Silicosis'. The booklet embodied reports by some of the leading research workers.

The principal basic research on which present optimism is founded was conducted on animals. It proved that, while injections carrying aluminium dust were ineffective, inhalation of the dust had prophylactic and arrestive effects. The fact that inhalation of aluminium dust had no harmful effect on the lungs was also established. Clinical tests on selected human sufferers, who voluntarily submitted themselves for treatment, although not yet conclusive, have given encouraging indications that an effective method has been found of combating the disease. Considered now to be caused by chemical combination of the silica in fine quartz dust with the alkaline fluid in the lungs, silicosis has for a long time been a menace to workers in Australian quartz mines, and a major problem for mining companies and medical authorities. It has been particularly prevalent on the Bendigo field, in Victoria. Application of results of overseas research to Australian mines will represent a great step forward in improving the health of miners by removing the threat of this dread occupational disease. It is emphasized, of course, that aluminium therapy does not aim at displacing other means of preventing silicosis, such as dust control, improved ventilation, and general hygiene. These indirect measures should never be relaxed.

MEDICAL BOOKS

MESSRS. E. and S. LIVINGSTONE LTD., 16 and 17 Teviot Place, Edinburgh 1, have sent us a copy of their publication entitled 'Medical Books, April 1946', which is an illustrated catalogue of medical, surgical, nursing, dental and scientific books. Copies of this catalogue can be had on application to the publishers.

PHILIPS TECHNICAL REVIEW, JANUARY 1946

The publication of this valuable paper had to be discontinued in 1942 and it is only now after the liberation of Holland that this monthly is appearing again.

The leading article in the January 1946 number is on 'Sintered glass' by E. G. Dorgelo. The next article on 'An x-ray apparatus for contact therapy' is contributed by K. A. G. Hazou, J. M. Ledebor and J. H. von der Tuuk. This apparatus fulfils certain important requirements, i.e. a rapid decrease of the irradiation intensity under the skin in case of treatment of tumours at the skin surface.

Compared with depth therapy conditions in surface therapy are more favourable, which fact has been turned to advantage in the construction of a light and easily handled apparatus. The shape of the tube, being elongated and narrow, deviates considerably from the normal; the tube can be pressed by hand on the tumour direct (contact therapy) without any high voltage danger for the patient or the practitioner. The focus skin distance is 18 mm.; the own-filter is equivalent to only 0.2 aluminium.

The apparatus is fed by 50 kV direct current; the tube current is 2 mA. The irradiation intensity at the point of contact amounts to 7,000-8,000 röntgen per minute, so that a few minutes' treatment is mostly sufficient. In dealing with the practical application of the apparatus the writers of the article point out, i.e. the high percentage of cures with contact therapy, the advantages of this method of x-ray treatment of tumours in cavities of the body and the possibility of making certain internal tumours accessible for contact therapy by means of operational exposure.

There are two more articles, one on 'The measurement of impedances particularly on decimetre waves' by J. M. van Hofweegen, and the other on 'An apparatus for stroboscopic observation' by S. L. de Bruin.

EIGHTH CLINICAL MEETING OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE HELD ON THE 1ST MAY, 1946

DR. A. K. M. ABDUL WAHED showed a case of a boy aged 12 years admitted to hospital for continuous pyrexia of 14 days' duration. The patient had an attack of pneumonia one year ago and had passed roundworms six months later. Enquiry showed that the boy was exceptionally backward in play on account of breathlessness. His legs had been weak since early childhood but his hands were quite strong. Mentally he was somewhat dull and was never put to school. On examination the patient was seen to be a thinly built boy with tortuous veins in the upper half of the abdomen. Pulsations of the superior epigastric arteries at the xiphisternum, of the internal mammary arteries in the 3rd, 4th and 5th intercostal spaces near the right and left borders of the sternum, etc., were visible. The carotid pulsation was vigorous. Examination of the pulse gave the idea of hypertension and no two pulses were equal. The femoral and the dorsalis pedis arteries revealed no pulsation. The heart showed the apex beat in the left 5th intercostal space in the anterior axillary line. The apical impulse was heaving in character. A systolic thrill was felt in the pulmonary area. The left and right borders of the heart were out. A systolic murmur was heard all over the areas with maximum intensity over the pulmonary area. This was localized to the upper part of the left border of the heart. There was no cyanosis and no clubbing of fingers. Blood pressure was 166/108 mm. Hg. There was congestion at the base of both lungs. The liver was palpable two fingers below the costal margin, tender and soft. The spleen was not palpable. The urine was negative. The blood picture showed haemoglobin 42 per cent (Hellige), erythrocytes about 3 millions per c.mm., white cells 3.7 thousand per c.mm. The sedimentation rate was 39 mm. per hour. The blood culture, Widal and W.R. were negative. Electrocardiogram showed left axis deviation with normal

sinus rhythm. From the history and the physical findings the case was diagnosed to be one of coarctation of aorta. In this disease the narrowing takes place after the origin of the left subclavian artery proximal to or at about the insertion of the ductus arteriosus. In the former which is known as the 'infantile' variety the ductus arteriosus is patent in the majority of cases and the pulsating blood vessels in the chest wall are not seen. In the latter which is known as the 'adult' variety the ductus arteriosus is usually obliterated and the pulsating blood vessels are prominent. In the present case the adult variety was found in a child. In coarctation we usually find a good physique and active mind unlike in the present case. There was no proof yet of subacute bacterial endocarditis.

Dr. Probodh Das described a case of elephantiasis of the vulva in a Hindu female, aged 30, mother of two children. Both pregnancies were normal but immediately after the second delivery 3 years ago, she was attacked with high fever and generalized swelling including her private parts. This was accompanied by enlargement of lymph glands and appearance of red 'streaks' in the limbs. The temperature, swelling, etc., subsided with treatment, excepting that over the vulva. Since then the patient has been having fever periodic with every full moon and new moon. After each attack of fever the swelling of the private parts increased till it has attained its present size. The patient was well developed and slightly obese. There was a round and globular swelling of the size and shape of an adult human hand growing from the right labia majus and minus and the adjoining portions of the *mons veneris*. The skin over the swelling was greatly thickened and corrugated resembling an elephantoid growth, with no sign of ulceration anywhere. The left labia majus and minus were very slightly thickened. The vaginal outlet appeared normal, admitting two fingers easily. Cervix was normal. The uterus was normal in size, mobile, retroverted and retroflexed. Tubes and ovaries not felt. Nothing abnormal detected per speculum. Laboratory examinations of blood, urine, etc., showed no abnormality except a slight anaemia. As pre-operative treatment the patient was given calcium and alkalies by mouth. After a few days she had an attack of fever which was controlled by sulphonamides by mouth for four days. A course of 'Filicid' injections, stimulant mixture and multivitamin tablets were then given. Under general anaesthesia the growth was removed by an elliptical incision through the base of the thick pedicle. As far as possible all the blubbery tissues from the base were removed. On section the tissues presented a pearly white, oedematous appearance with clear serous fluid exuding when pressed, like the typical blubbery tissues of filarial elephantiasis. On histological examination there was marked preponderance of the connective tissue with round celled infiltration arranged in groups. Blood vessels were absent except a few showing obliterative endarteritis. Epithelial lining was normal. The incidence of the disease, classification of types, diagnosis and differential diagnosis were discussed.

Dr. C. R. Das Gupta discussed the use of folic acid in macrocytic anaemia. A small supply of folic acid was made available by Dr. R. W. Linton of the Lederle Laboratories which was tried on 6 cases of macrocytic anaemia. The initial red cell count in all the cases was either below or just above one million per c.mm. Sternal marrow was plastic and megaloblastic in 5 and dimorphic in 1. Fractional gastric analysis showed absolute achlorhydria in 4, pseudoachlorhydria in 1 and hypochlorhydria in 1. No associated infection was detectable in any of the cases. Folic acid was given orally in doses of 20, 30 and 100 mg. daily, continually or with interruptions for varying periods. The case with dimorphic marrow did not show any improvement with folic acid but improved later with liver, iron and transfusion. Of the remaining 5 cases, one showed signs of acute abdomen on the 4th day of folic acid treatment and died. The 4 others showed definite improvement, clinically and haematologically. Transfusion of 300 c.c. of blood was given to one of these

cases on account of the very low condition. A fairly good reticulocyte response was noted in all the cases between the 4th and 6th day of treatment. In all the cases the improvement was sub-maximal and the blood picture continued to be macrocytic in character.

Dr. John Lowe showed a case of hepato-pulmonary fistula. The patient was admitted to hospital with what appeared to be an ordinary amoebic liver abscess. It was treated by repeated aspiration and emetine. There were to begin with no signs in the right lung or pleural cavity. At the first aspiration 1½ pints of pus were removed. At the second aspiration after a similar amount of pus had been removed, much air was aspirated from the liver. X-ray examination revealed a cavity in the upper part of the right lobe of the liver half full of pus and half full of air, the air being apparently sucked into the liver from the lung during aspiration. There was no coughing up of pus, so the opening apparently allowed air to pass downward but did not allow it to pass upward. Further attempts at aspiration produced only a little pus and a lot of air. Later the patient began to cough up amoebic liver pus but in spite of the treatment the drainage was inadequate and the patient had to be referred for surgical treatment. The treatment of the patient was handicapped by the fact that emetine induced marked cardiac symptoms. X-ray films showing the abscess cavity with pus below and air above were shown.

Dr. R. N. Chaudhuri showed a specimen of carcinoma of the transverse colon removed from a man aged 60 years who came in for dysenteric symptoms of 6 weeks' duration. The skiagrams were demonstrated showing the abnormal appearances. The tumour was removed successfully, but subsequently the patient died of right heart failure. Dr. Chaudhuri also showed a case of malnutrition with well-defined Bitot's spots in a boy aged 9 years. There was dermatosis of the crazy pavement type as well as generalized oedema due to hypo-proteinemia.

Professor G. Panja discussed the diagnosis in a case of cutaneous soft circumscribed swellings on the scalp, chest, buttocks, extremities and joints of about a month's duration with pain and tenderness in a Hindu female aged 17, married but without any issue. The patient had malaria 1½ years ago and 'typhoid' 4 months ago which subsequently developed into kala-azar and was treated with intravenous injection of organic antimony compounds. The family history revealed nothing of importance. About a month back the patient had an attack of measles associated with fever and the swellings appeared 2-3 days later. Fever subsided but the swellings persisted with pain and tenderness. Now pain is absent in some and less in others. The swellings are symmetrical in some regions, very prominent in some, and tender in some. Patient suffers from occasional nausea and headache, dimness of vision and weakness. Menstrual history regular. Sex organs normal. Scalp hair luxuriant. Skin moist. No goitre. Pulse 110-120 per minute. Blood pressure 85/50. Heart sounds weak. Lungs normal. Spleen enlarged, moderately hard, rounded border. Liver palpable. Throat septic. No anaesthesia anywhere. Skiagram of the skull showed normal sella turcica, no erosion at the base, and clinoid processes approaching each other. The blood count showed a low erythrocyte count. The sedimentation rate was high. W.R. doubtful. Antimony test and complement fixation test for kala-azar positive. The blood sugar was low and the glucose tolerance test gave a high figure. Other laboratory examinations were normal. On biopsy soft fibrous tissue with small cysts were seen here and there. Histological examination showed soft fibrous tissue with numerous fibroblasts and collagen bundles. At places myxomatous tissue was also seen. There appeared to be a cyst at one place. Newly formed blood vessels and dilated lymphatics and perivascular infiltration with small round cells were also seen. Culture from a swelling was sterile. Dercum (1892) described 3 cases (adiposis dolorosa) from Philadelphia Hospital, in patients aged 51 to 64, all very fat and with marked

psychic disturbances. The swellings were big, some 7 inches deep, present on arms, thighs, hips and pubis, but none on scalp and trunk; there were paroxysms of stabbing pain in the masses; anæsthetic areas were present in all the 3 cases. Dercum could not have a histological report of the tumours but he was certain that they were fatty in nature. In this case many of these signs and symptoms were absent, the patient was only 17 years, rather lean and thin, the tumours small and some present on trunk and scalp; not much pain and no anæsthesia and psychic disturbances; and the tumours were not fatty. The points against the diagnosis of neurofibroma were that the tumours were of recent origin and on section no nerve fibrils were found passing through and no jelly-like hyalin degeneration was seen. Besides all the tumours disappeared with treatment. The tumours were not perineural fibroma as there were no palisading and whorls of fibrous tissue. It is possible that they were of virus origin. They started after an eruptive fever of virus origin. There was some perivascular infiltration with round cells and the tumours disappeared gradually. Dr. Seal instanced a similar case after an attack of an eruptive fever. In treatment, sodium salicylate mixture, aperient mixture, sterodin injection and chemotherapy, paint and gargle for throat were given. The tumours all disappeared in 2 months, the patient improved much in health but an almost solid cedema of forearms, wrists, lower legs, feet and face appeared and persisted. Cedema was tender on pressure. There was also headache.

QUARANTINE RESTRICTIONS, ETC.

INFORMATION has been received by the Public Health Commissioner with the Government of India that the Governments of Sarawak and Philippine Islands have imposed quarantine restrictions on account of smallpox and cholera against arrivals from India by sea and air; by the Government of the Dutch East Indies on account of smallpox, cholera, typhoid and para-typhoid against passengers disembarking at or in transit through Sourabaya; by the Government of Palestine on account of smallpox against arrivals from Delhi and Allahabad by air; by the Government of Egypt on account of cholera against arrivals from India by air; and, by the Government of Hong Kong on account of cholera against arrivals from Calcutta by sea and air. In order to avoid possible delay and inconvenience on entry into the country concerned, passengers leaving India by sea and air for Sarawak and Philippine Islands are advised to be in possession of the following certificates:—

(1) Certificates of vaccination against smallpox showing that the vaccination has been performed not less than 14 days and not more than one year prior to arrival in the country concerned unless they bear evidence of a previous attack of smallpox or show local signs of an early vaccination reaction indicating adequate immunity;

(2) Certificates of inoculation against cholera showing that inoculation has been performed not less than six days and not more than six months prior to arrival in the country concerned.

(3) The certificate of inoculation against typhoid and para-typhoid fevers should not be more than one year old.

The Governments of Singapore Colony and of the Malayan Union have imposed quarantine restrictions on account of smallpox against passengers arriving from Madras by sea and air.

In the case of passengers leaving Delhi by air, Chittagong by sea and Bombay and Calcutta by sea and air for Malayan Union and Singapore Colony, the smallpox vaccination certificate should show that the vaccination has been performed not less than 14 days and not more than one year (not three years as previously announced) prior to arrival in these countries.

Similar restrictions have been imposed by the Government of Labuan (British Borneo) against arrivals

from Bombay and Madras, and on account of cholera against arrivals from Calcutta.

All persons intending to go to Afghanistan are advised to be in possession of cholera inoculation certificates showing that inoculation has been performed not less than six days and not more than six months prior to arrival in Afghanistan.

BRITISH COMMONWEALTH AND EMPIRE TUBERCULOSIS CONFERENCE, MIDSUMMER, 1947

THE National Association for the Prevention of Tuberculosis proposes to hold in London, in mid-summer, 1947, a conference dealing with tuberculosis in all its aspects. This conference will probably last three days, and invitations will be sent to representatives from the British Commonwealth and Empire.

There will be visitors also from the United States and from some European countries, and this direct exchange of ideas will promote a closer contact between various countries and the local health authorities responsible for tuberculosis in Britain.

The Duchess of Portland, Chairman of the Association, will preside at the conference.

ANTI-TUBERCULOSIS CHALLENGE SHIELD

THE Tuberculosis Association of India, New Delhi, awards the Hassan Masud Suhrawardy Memorial Anti-Tuberculosis Challenge Shield annually to the organization or institution which has the best record of effective anti-tuberculosis work done within that year.

Competition for this shield is open to corporations, municipalities, affiliated tuberculosis associations, district or local and other recognized bodies doing anti-tuberculosis work on approved modern lines.

THE PRINCE BIJEY SINGHJI MEMORIAL GENERAL HOSPITALS, BIKANER

THE Prince Bijey Singhji Memorial General Hospitals of Bikaner have been recognized by the Royal College of Surgeons of England under conditions of paragraph 23(b) of the Regulations for the Fellowship in respect of the posts of three general house surgeons.

Medical graduates desirous to obtain a house surgeonship may get in touch with the Principal Medical Officer, Bikaner.

34TH ALL-INDIA MEDICAL LICENTIATES' CONFERENCE, POONA, 1946

THE 34th All-India Medical Licentiates' Conference will be held in Poona on 19th, 20th and 21st October, 1946.

There will be a scientific section where papers on medical and scientific subjects will be read, and also a symposium on 'The problems of nutrition in India'. Members are requested to send their papers before the 1st October, 1946, to the Scientific Committee.

A medical and scientific exhibition is also being arranged in connection with the conference.

For further information please write to the Secretaries, Reception Committee Office, 502, Narayan Peth, Poona City.

CORRIGENDUM

OCULAR MANIFESTATIONS OF AVITAMINOSIS IN ADULTS

By M. N. SARDANA, M.B., B.S. (Pb.), L.R.C.P. (Lond.), M.R.C.S.* (Eng.), D.T.M. (L'pool), D.O.M.S. (Eng.), F.R.F.P.S. (Glas.)

MAJOR, I.M.S.

(I.M.G., 81, No. 4-5, p. 188.)

* Printed M.R.C.P. (Eng.) by error.

Public Health Section

A NOTE ON CHOLERA OUTBREAKS (1944-45) IN THE SINGUR HEALTH CENTRE AREA, BÈNGAL, WITH SPECIAL REFERENCE TO CONTROL MEASURES *

By S. C. SEAL, M.B., D.P.H., F.A.P.H.A.

(Assistant Professor of Epidemiology, All-India Institute of Hygiene and Public Health, Calcutta)

THE Singur Health Centre consisting of four Union Boards, viz, Singur, Balarambati, Bora and Begumpur (see map) in the district of Hooghly, Bengal, with an area of 33 square miles and 63,000 population, came under the present system of health organization in January 1944. Since then the area has been utilized by the All-India Institute of Hygiene and Public Health, Calcutta, for various field studies under rural conditions. In this connection the author investigated into the local cholera outbreaks with a view to evolving some simpler but efficient method of control within the means of the local health organization and the community.

Twenty-four of the 27 outbreaks of cholera in the area between 19th April, 1944, and 30th April, 1945 (roughly 1 year) were studied, the various areas of outbreak having been visited at different stages of the epidemic depending upon the interval of time that elapsed between the occurrence of the first case and the actual field visit. This has permitted a comparative study of the effects of certain control measures on these outbreaks at their different phases, from which some general principles of the method of control of cholera in the rural areas of Bengal have been developed. These will be described presently. A brief account of the outbreaks has been given in table I arranged according to the descending order of interval of time elapsing between the onset and the first field visit.

It will be seen from table I that within the course of a year as many as 17 villages (25 per cent) in the area were affected with cholera. The villages Ratanpur and Pahlampur had three outbreaks each, Biramnagar and Baruipara had two each and the rest had single outbreaks only. The total number of cases was 203 with 51 deaths, the case fatality rate being 25 per cent. The frequency distribution of cases in these outbreaks was as follows:—

Number of cases between	40 and 50	30 and 40	20 and 30	10 and 20	5 and 10	1 and 5	Single cases
Number of outbreaks ..	1	nil	1	4	9	3	6

* Presented before the Medical and Veterinary Section of the 33rd session of the Indian Science Congress, held at Bangalore on the 2nd January, 1946.

The duration of these outbreaks varied from a day or two to 50 days, the average being 10.6 days. The investigation accompanied by control measures was undertaken at varying intervals in different outbreaks, starting within a few hours to as long as 35 days after the onset, the average interval being 7.5 days. Definite history of importation was elicited in 13 outbreaks and probable importation in another 4. The other suspected sources or agencies were local *mela* 1 and contaminated milk 1, while no definite source could be elicited in 5 of them. *Melas*, *hats* and industrial centres are a few of the potent focal points from which cholera is generally imported into the area. Water does not seem to take any noticeable part in these outbreaks except occasionally in spreading the disease for a short while within a limited area through the use of the infected *dobas*. Direct contact and flies, on the other hand, seem to play more definite rôle in the local spread.

Results of the application of certain control measures

The gross fatality rate is 25 per cent for the series of outbreaks reported here. This will appear high if the effect of the control measures is judged without the details. The most important single factor in the control of cholera is *notification*. It will be noticed from table I that in certain cases the information was received very late; for instance, in the case of Panchghora outbreak it was delayed for as many as 35 days with the result that the epidemic had spread widely and 30 cases with 8 deaths (26.6 per cent) had already occurred before any control measure was actually instituted. Even so, 14 more cases had occurred before the final curtain could be drawn over this epidemic, although only one of them died.

The average duration of the outbreaks was 10½ days and the average interval between the onset and notification was 7½ days. In other words, roughly three-fourths of the cases had already occurred before the information was received. Thus of the 203 cases 157 or 77.3 per cent actually occurred before notification and only 46 or 22.7 per cent after the party's visit. Also of the 51 deaths recorded as many as 45 or 88.2 per cent occurred before the control

measures were adopted, and only 6 or 11.8 per cent afterwards. Translated into fatality rates these were 28.7 and 13.0 per cent respectively.

TABLE I

A brief account of the cholera outbreaks in the Singur Health Centre Area (1944-45) arranged in descending order of interval between the onset and the first field visit

Interval between first case and first field visit	Affected villages	OUTBREAKS			TOTAL		BEFORE NOTIFICATION		AFTER FIRST FIELD VISIT		Types of vibrio isolated	Probable source or mode of transmission
		Serial number	Date of onset	Duration, days	Cases	Deaths (%)	Cases	Deaths (%)	Cases	Deaths (%)		
35 days	Panchghora	4	21-7-44	50	44	9 (20.4)	30	8 (26.6)	14	1 (7.0)	Ogawa	Imported from Belur (an industrial centre). No definite source elicited.
22 "	Ratanpur	1	28-3-44	22	9	4 (44.4)	9	4 (44.4)	0	0	NAG	Imported from <i>Rash mela</i> .
18 "	Kamlapur	10	6-11-44	22	12	4 (33.3)	9	3 (33.3)	3	1 (33.3)	Ogawa	Do.
15 "	Begumpur	9	6-11-44	20	21	7 (33.3)	18	6 (33.3)	3	1 (33.3)	Do.	Imported from Panchghora outbreak.
13 "	Adan	5	17-8-44	19	14	2 (14.2)	10	1 (10.0)	4	1 (25.0)	Do.	No definite source elicited.
11 "	Serampore	13	28-11-44	13	15	4 (26.6)	13	4 (30.7)	2	0	Do.	Imported from <i>Jhulanjatra mela</i> .
10 "	Baruipara	3	12-8-44	13	7	1 (14.2)	5	1 (20.0)	2	0	Inaba	Imported from Shiakhala <i>hat</i> .
10 "	Basubati West	22	14-4-45	13	8	2 (25.0)	7	2 (28.0)	1	0	Ogawa	Imported by pilgrims arriving from Brindaban.
8 "	Beraberi	15	11-3-45	10	6	1 (16.6)	5	1 (20.0)	1	0	Do.	? Imported from Sheorafuli <i>hat</i> .
7 "	Pahlampur	14	28-12-44	8	6	2 (33.3)	6	2 (33.3)	0	0	Do.	? Do.
6 "	Do.	18	29-3-45	5	6	1 (16.6)	6	1 (16.6)	0	0	Do.	Imported from Basubati West outbreak.
6 "	Basubati North	24	30-4-45	7	8	4 (50.0)	8	4 (50.0)	0	0	Do.	No definite source elicited.
4 "	Mahamadpur South.	7	29-9-44	7	3	0	2	0	1	0	Sample spoiled	Imported by a child coming from another village.
4 "	Jagatnagar	8	28-10-44	11	9	1 (11.1)	6	0	3	1 (33.3)	Ogawa	? Imported from Sheorafuli <i>hat</i> .
3 "	Pahlampur	12	27-11-44	4	2	1 (50.0)	2	1 (50.0)	0	0	No sample	Imported from Bora 'and spread through a feast.
3 "	Baruipara	23*	23-4-45	11	19	6 (31.5)	9	5 (55.5)	10	1 (10.0)	Ogawa	Local <i>Charak mela</i> .
2 "	Biramnagar	2	20-4-44	10	5	0	3	0	2	0	Do.	No definite source elicited.
2 "	Ratanpur	19	3-4-45	1	1	0	1	0	0	0	Do.	Imported from Calcutta.
1 day	Bankipur	21	18-4-45	1	1	0	1	0	0	0	Do.	Imported from Konnagar (an industrial centre).
1 "	Bora Bazar	11	23-11-44	2	3	2 (66.6)	3	2 (66.5)	0	0	No sample	Milk obtained from a cholera infected house.
12 hours	Ratanpur	16	19-3-45	1	1	0	1	0	0	0	Ogawa	? Imported from Sheorafuli <i>hat</i> .
8 "	Ber	20	5-4-45	1	1	0	1	0	0	0	Do.	No definite source elicited.
6 "	Paltagar	17	26-3-45	1	1	0	1	0	0	0	Negative	Imported from Panchghora outbreak.
4 "	Bankagacha	6	29-8-44	1	1	0	1	0	0	0	Ogawa	
					203	51 (25.1)	157	45 (28.7)	46	6 (13.0)		

* See special remarks in the text.

The X^2 value being 5.2 the difference between the two rates is significant even for 2 per cent level and this has been achieved in spite of the delay in reporting and adoption of simple measures. Of the six deaths that occurred after the field party's visit only one case at Begumpur, a male child in whom cholera was superimposed on chronic dysentery, died when the case was in hand; the rest of the cases, one each at Panchghora, Adan, Jagatnagar, Kamalapur and Baruipara, died within a few hours of attack before any relief could be given.

It may be mentioned here that, though very few, some patients or families were at the beginning reluctant both in accepting the medical relief and in instituting the suggested control measures out of suspicion, ignorance or misrepresentation by some interested parties. However, more than a year's work in the Singur Health Centre Area has now largely removed this handicap.

It will also be seen from table I that whenever there had been a longer delay in instituting measures of control the spread was usually wider and the fatality rate higher than when an immediate notification was followed by prompt measures. This has been shown graphically in the chart.

An exception to this general trend of events will be noted in the Baruipara outbreak (outbreak no. 23). Although the information was received in this case only 3 days after the onset

by which time 9 cases had already been registered, 10 more cases occurred after the field party's visit. This happened mainly under the following circumstances: In the last few

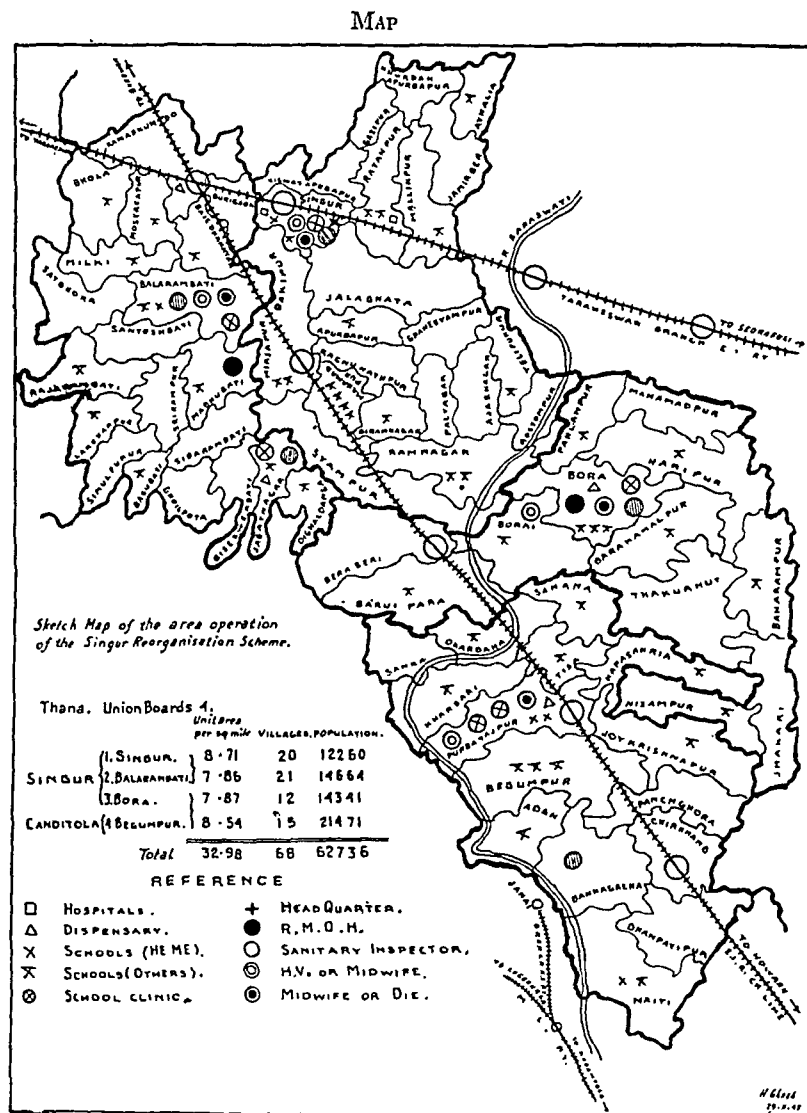


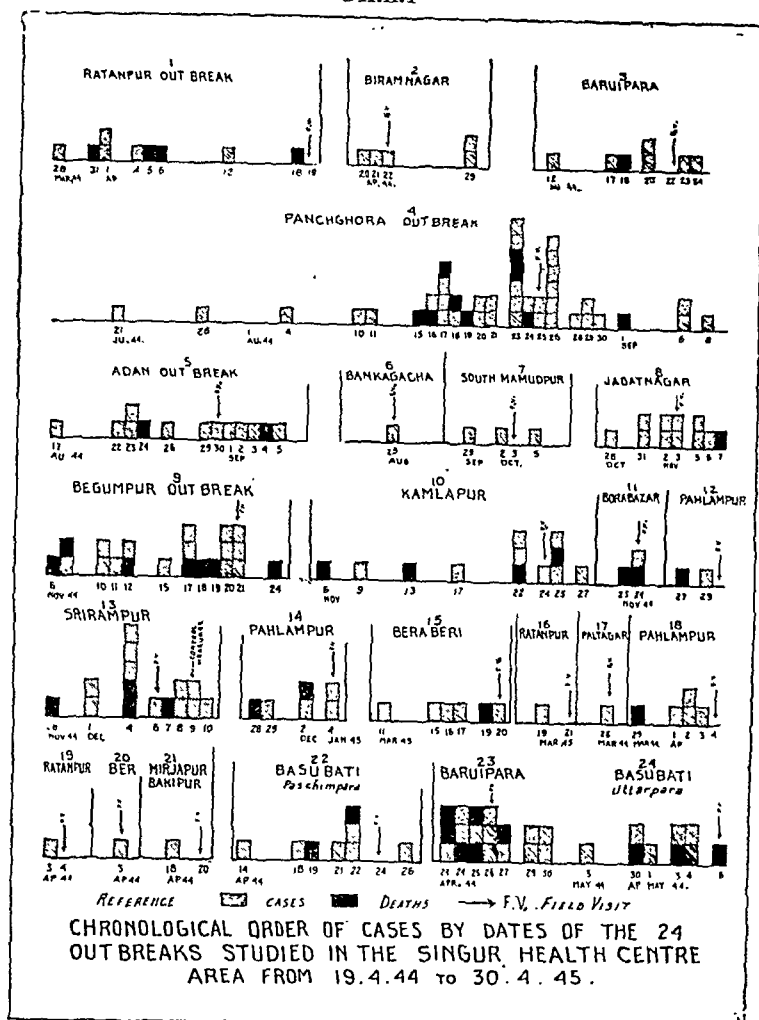
TABLE II
A brief account of the Haripur outbreak

Village	Duration of outbreak	Date of reporting	Interval between first case and field visit	Number of cases	Number of deaths	Number of families affected	Probable source
Haripur	24-7-45 to 23-8-45 (31 days).	13-8-45	20 days	24	2	16	Rathajatra mela at Mahesh near Serampore.
Mahamadpur	4-8-45 to 7-8-45 (4 days).	13-8-45	9 "	4	1	4	Haripur outbreak.
Pahlampur	9-8-45 to 14-8-45 (6 days).	11-8-45	2 "	15	5	12	Do.
TOTAL				43	8	32	

outbreaks, as will be seen from table I, there was definite improvement in notification and institution of control measures. The number of cases had also dropped much below the average (8 to

had involved at least two other neighbouring villages affecting 32 families. There were 43 cases in all, with 8 deaths, the mortality rate being 18.5 per cent.

CHART



9 cases). In order to find out whether it was due to the effect of more prompt control measures the latter were purposely relaxed for a while keeping an eye on the serious cases. A definite trend towards an increase in the number of cases was noted. This may also be seen in the following outbreak.

Cholera broke out in the village Haripur of Bora Union (*vide* map). The first case occurred on 24th July, 1945, but it was not notified until the infection had spread into some of the neighbouring villages, *viz.* Pahlampur and Mahamadpur. A brief description of this outbreak is given in table II.

It will be seen from table II that the first notification was received not from Haripur, the village originally affected, but from Pahlampur, a contiguous village into which the infection later extended, perhaps because the initial intensity was greater than usual. In fact, the information from Haripur was received 20 days after the first case, and the result was that no control measure other than the sporadic anti-cholera inoculation was adopted till the outbreak

Actual measures taken

The field party consisting of a medical officer, a supervisor and a sample collector (sweeper) visited the area at the earliest possible moment after the receipt of the information (usually within 24 hours). The following articles were carried by them to the field: (1) bleaching powder, (2) acid mixture, (3) a stock of sulphaguanidine, (4) anti-cholera vaccine with inoculation outfit (usually carried by the sanitary inspector attached to the Union), (5) sample collecting outfit, and (6) schedules for investigation and recording. Bicycles or the local train services were used to reach the villages and sometimes the whole or a part of the distance had to be covered on foot particularly when the road was too bad for cycling. In the same way the samples for bacteriological examination were sent to the Singur Field Laboratory.

Immediately on arrival at the village the party first made contact with the reported case or cases. A provisional diagnosis was made from the clinical signs and symptoms and from the character of stool and vomit. Once in a while, non-cholera cases, *e.g.* algid type of malaria, were reported as cholera but the number of such cases was negligible. The patient was attended first and if not already

convalescing a course of treatment with sulphaguanidine (initial dose 3 to 5 grammes followed by similar or smaller doses every 4 hours or more frequently) was at once started with the consent of the medical attendant, if any. Very often the available medical attention was meagre and cases unable to afford any were not few. In the author's experience, it was only on rare occasions that the treatment with intravenous saline was necessary if sulphaguanidine had been administered fairly early. The results of treatment under field conditions with this drug will be reported separately.

Arrangements were then made to isolate the patient as far as practicable, usually on a verandah in preference to a room. Methods of nursing the patient, of collection and safe disposal of patient's excreta, vomit and other fomites, and of disinfection with bleaching powder were actually demonstrated. The patient's immediate surroundings and other likely soiled places were disinfected with bleaching powder. This had immediate reaction on the flies which tended to keep themselves away,

at least as long as the chlorine effect lasted. The members of the household were then told about the danger generally caused by the flies in case of cholera infection and were instructed to spread the bleaching powder solution in and around the house at least twice during the day time. The villagers, out of tradition, themselves made arrangement for keeping the patient warm by constantly running a small fireplace nearby.

At this stage the schedules in connection with epidemiological investigations, *e.g.* home visiting schedules, patient's schedule and treatment card, etc., were filled in as far as practicable. Acid mixture (acid sulph. aromat. 3 parts and spt. chloroform 1 part) was then distributed (20 minims in an ounce of water for adults) to all the contacts who were made to swallow it in presence of a field worker. A sufficient quantity of this mixture was then left with them with instruction to use it twice a day in doses prescribed for each. The contacts not complaining of any bowel trouble at the moment were given anti-cholera inoculation. A careful enquiry was then made of the places including tanks and *dobas* already contaminated by the patient's excreta and arrangement made for their disinfection. Usually, the sanitary inspector was in charge of carrying out this disinfection as well as mass anti-cholera inoculation in the locality. Only in case of a wider outbreak, as in Panchghora (outbreak no. 4—*vide* table I), that other health personnel were requisitioned for carrying out anti-cholera inoculation over a large area within a short time. It may be mentioned here that the response to this inoculation is generally poor except in people around the immediate neighbourhood of the cholera cases.

A small stock of sulphaguanidine powder in packets of one gramme each was also left with the household for use in case of any member showing symptoms during the absence of the field party.

In addition to the samples of stool and vomit from the patient samples of water from various suspected or obviously contaminated sources, *e.g.* tanks and *dobas*, and whenever possible of stools of contacts were regularly collected during the period of the outbreak for bacteriological examination.

Finally, before leaving the patient's house for the day, the following instructions were given and the importance of carrying them out strictly was emphasized :—

1. Administer sulphaguanidine according to the doses and intervals prescribed.
2. Give enough fluid to the patient in the form of *dab* water (green cocoanut), alkaline mixture, glucose, etc.
3. Keep the patient warm.
4. Call the local doctor if the patient takes a bad turn during the absence of the field party (the local practitioners generally co-operated in the matter, while few patients

preferred to remain exclusively under private medical care).

5. Keep bleaching powder solution (one teaspoonful of fresh powder in a gallon of water) in an earthen vessel always ready for washing hands of the attendant and for other disinfecting purposes.

6. Collect vomit and stool in earthen pans (*shara*, costing $\frac{1}{2}$ anna each) and to bury them immediately into a pit dug in the earth for the purpose, if possible after disinfecting with bleaching powder.

7. Disinfect the pan with strong bleaching powder solution in case the same pan is required to be used repeatedly.

8. Keep medicine and drinking glasses, utensils and other materials used by the patient or coming into contact with him strictly separate, to be finally buried, burnt or at least disinfected with bleaching powder before being released for general use.

9. Bury the food left by the patient and to burn or bury the soiled linen and beddings or to disinfect those meant for repeated use in bleaching powder solution followed by washing with tube well water over a dug pit.

10. *Never* wash anything in contact with a patient in a tank or *doba* or in any other water source.

11. Wash your hands in bleaching powder solution each time you handle some infected or infectious material such as soiled linen, vomit, stool, etc.; keep away from the kitchen and do not handle anything other than those belonging to the patient as long as you are in attendance, without thoroughly disinfecting the hands and, if possible, changing clothes.

12. Do not allow children to have any kind of food in close vicinity of the patient or to come and play near him or her; the adults not attending the patient are also to keep away from the patient as far as practicable, particularly those in charge of the kitchen.

13. Completely abandon the use of tank or *doba* water and instead use only tube well water for all household purposes and boiled water for drinking purposes, at least for the duration of the outbreak.

14. Carefully prepare and cover all foods, which are to be eaten hot as far as practicable, and do not drink milk without boiling nor indulge in any stale or preserved food (including water-preserved rice) and drink; wash your hands in disinfecting fluid followed by tube well water before taking any food or drink.

15. Avoid all irritant foods, cooked or raw, and drink from unknown sources, at least for the duration of the epidemic.

16. If a contact, take acid mixture twice daily in doses prescribed. In case of suspicious symptoms, *e.g.* nausea, uneasiness in abdomen, vomiting or diarrhoeic motion, rest completely, take at once a dose of sulphaguanidine and notify the field party at the earliest opportunity.

17. Treat all excreta related to the suspicious cases in the same way as that of cholera patient. Disinfect or cover with earth or ashes places already soiled with excreta and do not allow any *doba* or tank to be used for ablution purposes; inform the field party if such sources are already contaminated.

18. Ask relatives and friends to keep away from the house for the duration of the outbreak except those who come to nurse the patient and give track of visitors who had come and gone.

The following instruction was given for preserving the specimen for bacteriological examination :—

Collect the morning specimen of stool or vomit in a fresh earthen pan without any anti-septic and keep it completely covered with another earthen pan (usually supplied by the field party) or in its absence with a piece of banana leaf (plentiful in the locality) fixed under a small weight. (After collection of the sample this is properly disposed of by the field party.)

If any sample had to be collected during the absence of the field party the method of collecting it into a bottle containing preserving fluid (2 per cent alkaline NaCl solution) was actually demonstrated. Most of the villagers were able to do it without any difficulty. Similarly, the instructions stated above were generally followed, and in the actual experience of the author; secondary cases were rare except those already in the incubation period, mostly having abortive attacks.

After taking care of the affected houses one after another in the manner described above a search was made for the undetected cases by making house to house and other local enquiries. Attempts were also made to bring home to the villagers the highly infectious nature of the disease and the danger of a wider spread unless all of them gave active co-operation in the control work. They were given the following instructions in addition to those already mentioned in connection with the management of cholera patients and their contacts and surroundings :—

1. Immediately notify to the field party all fresh or suspicious cases.

2. Get all people in the village immediately inoculated.

3. Restrict the movement of the people belonging to the affected houses, and ask visitors to keep away from the village and particularly from the affected houses.

4. Suspend all local sweetmeat shops or eating houses for the duration of the outbreak.

5. Prevent any person from contaminating water sources, e.g. tube wells, *dobas* and tanks, and inform the field party about the sources as soon as any such contamination is suspected.

6. All families to use boiled water for drinking purposes, to abandon the use of tank and *doba* water for domestic purposes during the outbreak and to entirely prohibit the use particularly of those with history of contamination.

7. Cautiously diet the patient for a few days before allowing the normal diet.

8. Convalescent patients to take special precautions for a few weeks to avoid infecting others including his own family members.

The affected area was visited daily and the same operation continued till the epidemic was completely controlled. In the meantime, the investigation was completed by tracing out all cases in their chronological order till the first authentic case was detected. From the latter the probable original source of infection was elicited, and then by studying the history of cases, physiography of the village and related circumstances, the link between cases and the most probable or the common mode of spread was determined. A summary report was sent to the Administrator of the Singur Health Centre.

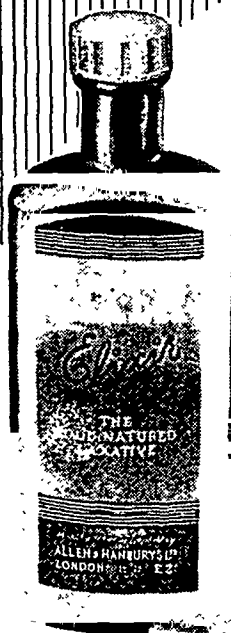
The above work was carried out only as a part of an enquiry into the gastro-intestinal disorders, whose main object was to find out the relationship of the incidence of various types of diarrhoeas and dysenteries to the existing water supplies in the area. Since the results of the control measures against cholera noted here were not the outcome of any special effort or organization it may be reasonably expected that the methods of control adopted in the local outbreaks mentioned above will be practicable in a set-up of public health organization like the one at Singur and are worthy of adequate trial.

Summary

Twenty-four of the 27 outbreaks of cholera involving 203 cases and 51 deaths between 19th April, 1944, and 30th April, 1945, in 17 out of 68 villages belonging to the recognized Singur Health Centre (Bengal), were investigated and control measures applied. Nearly three-fourths of the outbreaks could be traced to imported cases from neighbouring *melas* and industrial centres. The special feature was the use of sulphaguanidine and an acid mixture (acid sulph. aromat. 3 parts and spt. chloroform 1 part) in these outbreaks, the former proving effective as a therapeutic agent and the latter as a useful preventive in rural work.

The actual measures taken have been described in details. Early notification and prompt attendance to the affected areas proved as expected to be most essential prerequisites for the quickest suppression of the outbreaks. In general, it was found that the number of cases in an outbreak would be directly proportional to the delay in notification, and that after notification the mortality rate could be reduced to a low figure.

Thanks are due to Dr. J. B. Grant, C.B.E., the late Director of the All-India Institute of Hygiene and Public Health, Calcutta, for initiating the investigation, and to the field supervisor, Mr. Purnendu Chatterji, for his sincere devotion in this work. The drug, sulphaguanidine, was obtained through the courtesy of Rai Bahadur Dr. B. M. Das Gupta, formerly Director of the School of Tropical Medicine, Calcutta.



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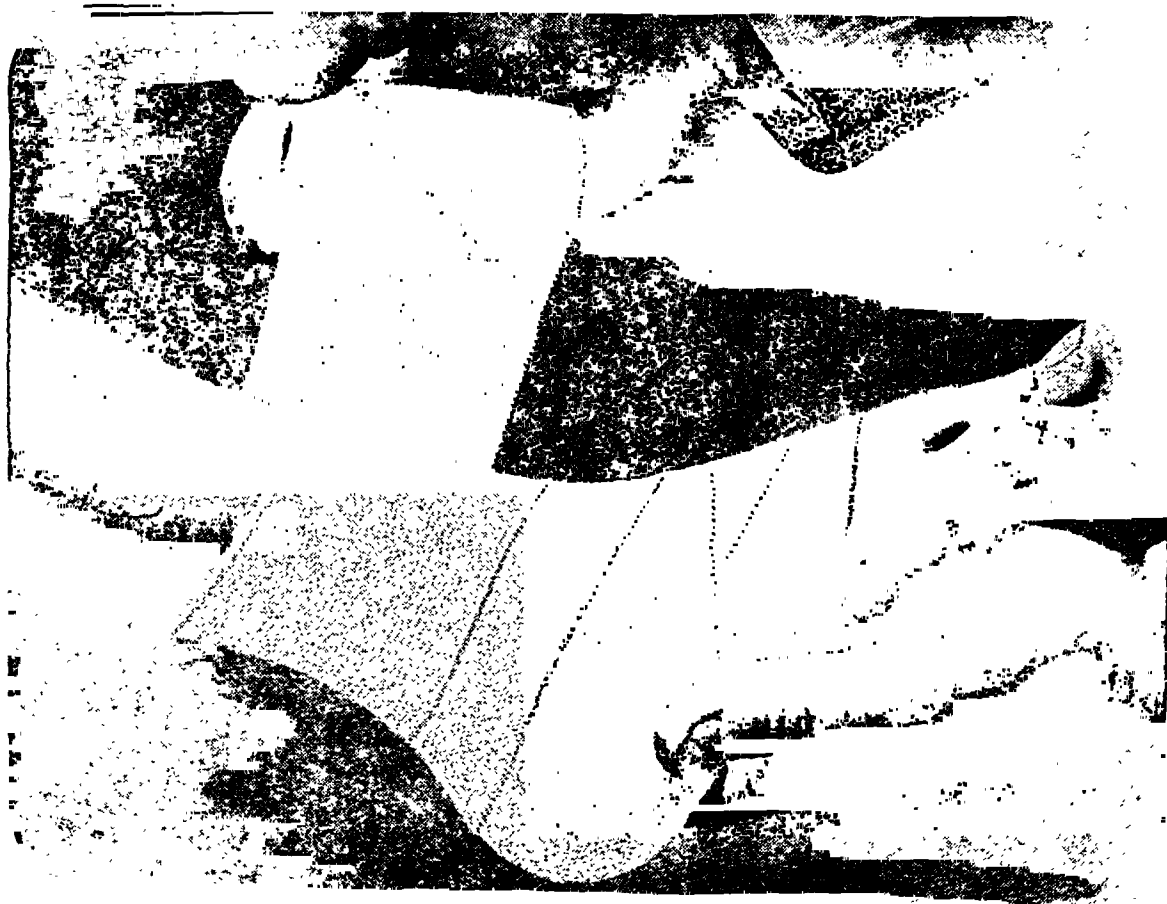
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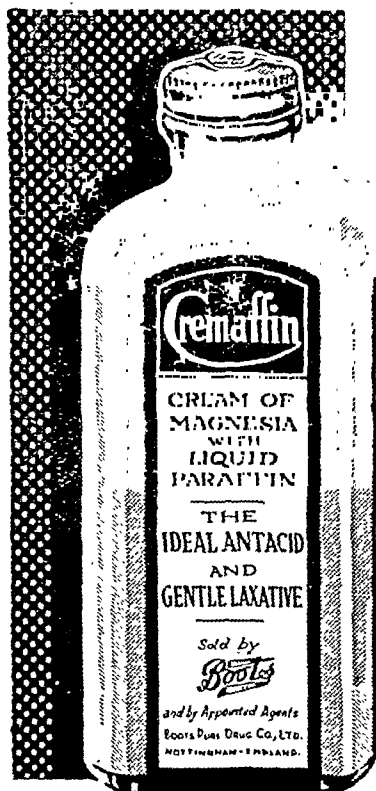
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Current Topics

Transfusion in the Treatment of Battle Casualties

By L. WHITBY

(Abstracted from the *Journal of the Royal Army Medical Corps*, Vol. 85, December 1945, p. 266)

The art of transfusion.—The art of transfusion lies in the selection of cases, the choice of correct fluids and their administration in appropriate volume at an optimum rate. Until the more elaborate methods of laboratory control have been reduced to bedside procedure, reliance has to be placed upon clinical judgment of the individual case; here the trained and experienced transfusion officer could obtain a desirable result with far less material and considerably less anxiety than his less experienced colleague.

As to selection of fluid: Here, one can do no more than indicate certain principles which should guide selection. The vital requirement in the majority is volume restoration. This can be accomplished with either blood, plasma or serum. At the same time, a man will stand an operation far better if his hæmoglobin is not below 60 to 70 per cent. A judicious mixture of blood and plasma will achieve this. And there is a great difference between fresh blood, young stored blood and old stored blood. If only the last named is available it is certainly not advisable to give huge quantities (part of which is inevitably hæmolyzed and so releases pigment into the circulation) to those who are potential candidates for renal failure. And, again, the impression at one time prevalent that abdominal wounds required huge quantities of blood has been contradicted by Grant's precise laboratory-controlled work, which has shown that the main danger is plasma loss rather than blood loss. Saline infusion has also become more widely practised, partly as the result of experience, partly from American influence.

The volume to be administered and the rate of administration are individual matters. Most medical officers know that massive limb injuries may require large volumes, five or six pints as a pre-operative measure, but some are still diffident of administering at a fast rate. Any one who has suffered a blood loss serious enough to demand instant transfusion, unless the injury is to the lung, cannot have the first three pints administered too fast. Unless the rate is fast, the response is often delayed and disappointing. With these, too, transfusion should not stop in the pre-operative ward; operation and the post-operative phase need to be supported, otherwise many deaths occur.

In principle, once a response has been elicited, the later transfusions are given in a volume and at a rate appropriate to the general condition. Of great importance is an appreciation of the urgency of surgery when tissue damage is massive. These cases can often be no more than partially restored by pre-operative transfusion. When this is so, when the patient seems to hang fire despite continued transfusion, then his only chance of life is to take the risk of immediate operation with a transfusion in progress. Likewise, with gross infection. Until the cause, the toxic focus, has been removed, little response to transfusion can be expected. Judicious transfusion has also a great place during convalescence.

Failures, disappointments and disasters.—A number of unsuitable cases have undoubtedly been submitted to the operation. Injuries to the brain and central nervous system respond poorly; unless there are serious injuries elsewhere, such cases are best left alone. Bone injuries now carry a risk which is recognized as relatively common; this is the precipitation of fat embolism, which should be suspected whenever unexplained pulmonary or cerebral symptoms arise during the transfusion of a case with a bone injury. The

transfusion should be stopped, as it tends to increase the amount of fat in the circulation; immobilization and rest are the only effective remedies.

Certain cases should never be transfused. These include thoracic injuries with an embarrassed circulation from hæmopericardium or other mechanical causes, and injuries to the lung alveoli from blast or irritant gases. Indeed the transfusion of any chest injury case should be undertaken with caution on account of the danger of pulmonary œdema. Disasters from incompatible blood have been almost unknown. This is a tribute to the complete group-checking system which was rigidly enforced, whereby both agglutinin and agglutinin content of all group O blood was carried out before release. Trouble has occasionally arisen from the use of massive quantities of somewhat old blood (*supra*) but the bogey of infected blood has appeared only on small occasions, despite the fact that the armies have operated in all climates and under most difficult conditions.

Real versus Supposed Disturbances of the Endocrine Glands

(Abstracted from the *Medical Journal of Australia*, Vol. 2, 29th December, 1945, p. 507)

MANY physicians living to-day have had the opportunity of witnessing the rise of endocrinology from small beginnings to a position commanding a large and ever-growing literature. That enthusiasm has led to an uncritical attitude in diagnosis and treatment is the thesis of Edward H. Rynearson. Dr. Rynearson utters a warning against the cocksure endocrine diagnosis of an abnormality for which another and simpler explanation can be found. 'Because myxœdema is a clear-cut entity caused by the lack of a single hormone the administration of a small amount of thyroid extract completely controls the condition'. The estimation of basal metabolic rate is an elegant procedure, giving a numerical assessment, but all patients with low basal metabolism are not sufferers from thyroid deficiency; blood count, blood pressure and the gastric acid content may be low too; 'dropped stomach', 'dropped colon', 'dropped kidneys' or a retroverted uterus may be present and the administration of thyroid extract in such states would not be of the slightest benefit, to put it mildly. Diabetes insipidus is a consequence of under-action of the posterior lobe of the pituitary, yet many nervous water drinkers have been classified as suffering from endocrine disorders despite the fact that the differential diagnosis is comparatively easy.

The boy who at school is nicknamed 'Fatty' often develops into a big and healthy man and has nothing the matter with his pituitary; similarly, girls over-tall for their years may require only philosophical adjustment to their height. Many a woman with undue adiposity and hairiness needs a prescribed scale of diet and exercise and a visit to a cosmetic specialist. The exhaustion of a tired businessman keeping his affairs going with inadequate staff is often regarded as showing a male menopause. Dr. Rynearson suggests that if such a man had fewer forms to fill up he might easily regain physical vigour and sexual potency. Most mental defectives and most psychopathic and psychoneurotic persons have no endocrine dysfunction at all. Dr. Rynearson's final conclusion is well worth a special mention: 'Obscure diseases usually are not made lucid by incriminating the endocrines'. That endocrine therapeutics has had some triumphs none will dispute, but there is a tendency to stretch out the list.

New Remedy for Lupus

(From the *Lancet*, i, 5th January, 1946, p. 23)

IN 1943, Dr. G. B. Dowling at St. Thomas's Hospital, began to treat lupus vulgaris with large doses of calciferol (vitamin D₂) by mouth. At meetings held by the section of dermatology of the Royal Society of

Medicine in the past two months he and Dr. E. W. Prosser Thomas of the same hospital have described remarkable results obtained in some of the 38 cases so far treated in this way, 16 of which have been followed for more than a year. Some of them had previously had x-ray therapy, and in these it has been harder to judge the response to the new remedy; but Dr. Dowling thinks it fair to say that all have improved under calciferol, and in a dozen the lesions seem to have entirely disappeared. In one patient there has been no return of the disease in the 18 months since treatment stopped; and though a few have shown little benefit, the majority have been strikingly improved by calciferol when they had made poor progress with other remedies. Members of the dermatological section, who saw some of the cases, were much impressed; and it was pointed out that the new form of treatment is far simpler and less expensive in time and effort than current methods such as frequent exposure to Finsen light or ultra-violet rays. On the other hand it has the disadvantage of employing doses which border on the toxic, and at least 8 patients have shown signs of intolerance such as nausea, loss of appetite, and depression. Most of these, though not all, were receiving 150,000 international units of calciferol daily, and in all of these symptoms of intolerance disappeared when the dosage was reduced to 100,000 I.U. Unlike the natural vitamin D₃, obtained from fish liver oils, calciferol is prepared artificially by irradiating a vegetable sterol ergosterol, and preparations may include other toxic by-products of irradiation. Very large doses are known to cause deposition of calcium in soft tissues—notably the renal tubules and arterioles and the media of large blood vessels—and though this abnormal calcification tends to disappear on discontinuing the use of calciferol, dosage on the scale used by Dowling and Prosser Thomas for lupus should not be employed without carefully considering the individual case and keeping a watch for toxic symptoms. This aspect of the subject is discussed more fully in the report of the November meeting to be published in the December issue of the *Proceedings of the Royal Society of Medicine*, now in the press. The meeting held on 20th December will be reported in a later issue of the society's proceedings.

Schistosomiasis: Intensive Treatment with Antimony

By W. ALVES

and

D. M. BLAIR

(Abstracted from the *Lancet*, i, 5th January, 1946, p. 9)

A HUNDRED cases of schistosomiasis have been treated with a two-day treatment using sodium antimonyl tartrate with a 'multiple syringe' technique.

No viable eggs were found in any case immediately after treatment or at two months and three months after treatment in the cases followed up.

In 53 cases followed up for two months the cercarial antigen skin test had become negative in all but 14 cases (73 per cent).

Nine of the 14 skin-test-positive cases were observed for three months and the test became negative in 6 cases in this period.

The method should facilitate mass treatment in the control of schistosomiasis.

Buffer Precipitation Test for Malaria

By E. BOGEN

(From the *U.S. Naval Medical Bulletin*, Vol. 45, July 1945, p. 47, as abstracted in the *Tropical Diseases Bulletin*, Vol. 42, November 1945, p. 861)

THE buffer precipitation test used by the author is based on an observation made by E. K. Wolff, that normal human blood serum added to distilled water

at pH 7.7 remains clear, but that blood serum from malaria patients becomes cloudy.

Small test tubes such as are used for the Kahn test are employed. Into one, 1 c.c. of Test Buffer Solution A is placed; this solution is made by adding one part of a stock buffer solution with a pH of 7.7 to four parts of distilled water and then adding 0.2 per cent formalin as a preservative. A second tube contains 1 c.c. of Control Solution B, consisting of one part of stock buffer solution pH 7, four parts of distilled water and five parts of isotonic sodium chloride solution with 0.2 per cent formalin. Two drops of the clear serum to be tested are placed in each tube. The tubes are then well shaken and left at room temperature for from half to two hours when the reaction is read. The tubes are compared; greater turbidity in Solution A as compared with Control Solution B indicates a positive reaction.

More than 3,000 such tests have confirmed the validity of the reaction. The reaction is strongest in active malaria between paroxysms and in recently recovered patients but it remains positive for many months. The test helps both in individual diagnosis and in the detection of malaria in large groups. It might help in prognosis, in guiding suppressive and therapeutic measures, and in evaluating cures. It might also be of assistance in epidemiological studies, by measuring the incidence of malaria infection in a community.

Pain in Pectoralis Minor

(From the *Lancet*, ii, 15th December, 1945, p. 785)

THE established case of angina pectoris is easily recognized, but the differential diagnosis in the early stages is becoming increasingly complicated. The latest condition to be described as simulating angina pectoris is strain of the pectoralis minor muscle, which, in the opinion of an American observer, ranks second to psychoneurosis and the anxiety state as a cause of precordial pain in men of military age. In such cases there may be no history of trauma, and the presenting symptom is pain, usually in the mid-clavicular region of the chest at the level of the 3rd, 4th and 5th ribs, sometimes radiating to the shoulder but never down the arm. The pain may be intermittent, and it may appear to be related to exertion, but careful investigation shows that this is only so if the effort involves movement of the upper limb. The pain can be reproduced by making the patient push the upper arm forward against resistance when the elbow is at the side and behind the axis of the body. There is tenderness over the pectoralis minor, maximal at the site of the pain, and injection of procaine at this site abolishes the pain. Heat, massage, and local rest usually bring relief within a few days, but in two cases the attacks of pain recurred over a period of years. It is suggested that the pain is due to rupture of the pectoralis minor at its insertion into the chest wall. This is by no means the first time that attention has been drawn to the rupture of muscle fibres or fibrositis in the differential diagnosis of angina pectoris, but it seems to be the first time that this particular lesion has been incriminated.

Two facts should always be remembered in examining suspected cases of angina pectoris: that a full and careful history is essential for correct diagnosis, and that the pain of angina is substernal.

Comparative Effect of Sulphonamide and Penicillin in Pneumonia

By T. ANDERSON

and

M. S. FERGUSON

(Abstracted from the *Lancet*, ii, 22nd December, 1945, p. 805)

A SERIES of 126 patients over the age of 35 years suffering from pneumonia was divided by random

selection into two groups, one of which was given sulphathiazole, the other penicillin. All patients received the same symptomatic treatment and general clinical control.

The distribution of factors known to influence the course of the disease was the same in the two groups.

Each method achieved fairly similar results. In 3 patients, however, it was thought that penicillin had produced an unexpected recovery.

There is no reason for abandoning properly controlled sulphonamide treatment for the average case; and it is suggested that penicillin should be used for selected patients, usually in combination with a sulphonamide.

Some tentative guides for the efficient use of penicillin may be formulated. In the first place, in such severe cases, an adequate dose of a sulphonamide should be given during the first twenty-four hours. In the second place, a preliminary blood culture (before administering sulphonamides) becomes of increasing importance; for a positive result, especially if the infection is heavy, should suggest the need for starting penicillin. Thirdly, a routine white cell count, when treatment is begun, will be of value in picking up the leucopenic patient (not uncommon in this age group) who may respond unsatisfactorily to sulphonamides. Lastly, but not least important, the clinical assessment of the patient should be taken into account. We are satisfied that a poor cardiovascular system remains the most important prognostic factor in pneumonia, and should constitute an indication for combined therapy. Extensive pulmonary involvement, severe cyanosis, and dyspnoea are other indications which may call for the support of chemotherapy by penicillin.

Phthalylsulphathiazole ('Sulphathalidine') : Clinical, Chemical and Bacteriologic Evaluations in Infectious Diseases of the Colon

By M. H. STREICHER

(Abstracted from the *Journal of the American Medical Association*, Vol. 129, 15th December, 1945, p. 1080)

1. PHTHALYLSULPHATHIAZOLE is efficacious in colon infections.
2. The new sulphonamide produced no toxic symptoms in 100 patients.
3. A dosage of 3 gm. daily is preferable to larger amounts.

Penicillin in Gonorrhoea

By S. M. LAIRD

and

A. B. FIELDSEND

(Abstracted from the *Lancet*, i, 1946, p. 53)

PENICILLIN has justified its early promise in gonococcal infection, but the problem has been to find a standard dosage which will produce most cures in the shortest time with the maximum amount of penicillin. The authors describe their results in 528 cases of acute uncomplicated gonorrhoea in service men, using ten different schedules of treatment. Best results were obtained by giving five intramuscular injections at intervals of two hours, and there seemed to be no advantages in giving 150,000 units rather than 100,000. The proportion of failures rose if the number of injections was reduced or if the interval between injections was increased to more than three hours. The proportion of successes was an appreciable improvement on results with sulphathiazole in 408 cases treated in the same hospital. The total dosage of this drug was 20 gm.; 10 gm. on the day of admission, followed by

5 gm. daily for two days combined with urethral irrigation and a high fluid intake. The only drawback in the report is that all the patients in the penicillin series did not complete the final tests made three months after leaving the hospital.

Medicolegal

Evidence held sufficient to show that Death caused by Tetanus arose out of the Deceased's Employment

(Abstracted from the *Journal of American Medical Association*, Vol. 131, 4th May, 1946, p. 68)

A WORKMAN died of tetanus infection following an onset which started two and one-half days previous to his death. An autopsy disclosed an abrasion on the tip of one finger of his right hand which had apparently healed. The widow testified that the deceased dressed this abrasion several times prior to his death and that it was an ugly jab caused by the slipping of a drill while he was remodelling a butcher shop about two weeks before he died. In the course of his job he had to handle old lumber, animals were butchered in the room in which he worked, and there were hides in the same room which he had to move out of his way. There was medical evidence that tetanus occurs frequently in the vicinity of animals, that manure is especially likely to contain tetanus germs, that unless the animals are kept clean the outside of the hides is apt to be infested and that dirt is a frequent source of tetanus infection. The wound on the deceased's finger showed no sign of local irritation or infection at the time of his death, but the medical evidence showed that this was not decisive in cases of tetanus. The supreme court held that while some people have tetanus germs within their bodies, particularly their intestinal tracts, and it is possible for the germs to cause a tetanus lesion without an outside wound, nevertheless the probability is the other way and a wound is the most likely place for the germs to enter. The history of this case, concluded the court, indicates the injured finger as the portal of infection and the hides as the source of the tetanus germs.

Drunkenness: Results of Chemical Tests of Blood taken from Unconscious Person—Use during Trial—Self-Incrimination

(Abstracted from the *Journal of American Medical Association*, Vol. 131, 4th May, 1946, p. 68)

A PERSON was convicted of manslaughter on a charge of operating a motor vehicle on a public highway while under the influence of intoxicating liquor and he appealed to the supreme court. After the accident out of which the charge of manslaughter arose, the defendant remained unconscious for about 48 hours. While unconscious he was arrested and taken into custody by the police and treated for his injuries. At the request of the police a sample of blood was taken for determining its alcoholic content which was reported to be 260 mg. per 100 c.c. The admission in evidence of this testimony was objected to primarily on the ground that the use of such testimony was a violation of the constitutional provision that no person shall be compelled in any criminal prosecution to testify against himself and that such testimony is to be taken as an admission or confession or as evidence of a physical examination. The court held that the protection from 'testifying', from 'furnishing evidence' or from 'being a witness' was provided in order to place beyond the reach of ordinary legislative alteration the privilege

against self-incrimination. Assuredly, the object of this protection is the employment of legal process to extract from the person's own lips an admission of his guilt which will thus take the place of other evidence. If the arrest of a prisoner is lawful, the officer making the arrest may search the person or the prisoner and take from him not only the instruments of the crime but also such articles as may be of use as evidence on the trial. For purposes of identification, an accused may be required to do many things without having his constitutional rights against self-incrimination invaded. He may also be fingerprinted, photographed and measured under the Bertillon system. In the present

case no motion was made for the return or the suppression of the blood sample and the evidence of the result of the analysis of the blood sample was obtained without the use of any process against him as a witness. He was not required to establish the authenticity, identity or origin of the blood. If this evidence is inadmissible, said the court, it is difficult to understand under what theory fingerprints procured under compulsion, or evidence concerning them, is admissible, and the justification for requiring the accused to do the other acts referred to. The court therefore held the testimony concerning the blood sample admissible.

Reviews

SYNOPSIS OF OBSTETRICS AND GYNÆCOLOGY.—

By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G. Ninth Edition. 1945. John Wright and Sons Limited, Bristol. Pp. vii plus 500, with numerous diagrams. Price, 21s.

THIS handbook is meant to prepare students for qualifying examinations in obstetrics and gynaecology. It is meant as a supplement and not as a substitute for ordinary textbooks. Its main use is for rapid revision. Controversial and extreme views have been avoided. The material is presented in the form of concise notes and there is an excellent index. There are 168 illustrations in the form of line drawings. It is an excellent book for the purpose for which it is intended.

A HEY GROVES' SYNOPSIS OF SURGERY.—Edited

by C. P. G. Wakeley, C.B., D.Sc., F.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. Twelfth Edition. 1945. Oxford University Press, London. Pp. viii plus 719

THIS is another book in the same series and of a similar nature, a book to enable the students rapidly to revise the subject for examination purposes. The book originally written by Hey Groves has been revised in this edition by C. P. G. Wakeley. An excellent book of its kind.

A MANUAL OF SURGICAL ANATOMY.—By Tom

Jones and W. C. Shepard. 1945. W. B. Saunders Co., Philadelphia. Pp. xvi plus 195. Illustrated. Price, 25s.

THIS book is one of a series prepared to furnish the medical department of the U.S. Army and Navy with a compact presentation of necessary information in the field of military surgery. The book has been supervised by a committee on surgery and the illustrations are by Jones and Shepard. The book consists of four parts, part 1 head and neck, part 2 trunk, thorax, abdomen and pelvis, part 3 upper extremity, and part 4 lower extremity. The book consists almost entirely of illustrations numbering altogether several hundreds, considerable use of colour being made in every picture. There is an explanatory index occupying over fifty pages. As a compact guide to surgical anatomy profusely and excellently illustrated it would be difficult to equal this excellent book.

ILLUSTRATIONS OF REGIONAL ANATOMY.—By

E. B. Jamieson, M.D. Complete volume, 7 sections. Sixth Edition. 1946. E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 320 plus 16. Price, 75s. net

THE last edition of this book was reviewed in this journal in 1944. This the sixth edition contains mainly minor alterations and improvements and it reaches us in one volume instead of in seven sections; the volume ends with a good index. This publication deserves the highest praise and this edition is better even than the last.

EXERCISES IN HUMAN PHYSIOLOGY.—By Sir

Thomas Lewis, C.B.E., F.R.S., M.D., D.Sc., LL.D., F.R.C.P. 1945. Macmillan and Company, Limited, St. Martin's St., London. Pp. xiv plus 103, with 8 illustrations. Price, 3s. 6d.

THE author has correctly stated that the transition from preclinical to clinical studies is the most difficult period through which medical students have to pass. The book clearly elucidates the physiological principles applied to the patients in clinical studies.

The book is divided into 33 headings which are further subdivided into suitable subheadings, each in itself comprising an exercise. Wherever necessary, these exercises are suitably commented upon and each heading is followed by an 'application', explaining clearly the principles involved in those exercises. The author has all along emphasized the usefulness of simple bedside methods in demonstrating the physiological principles as seen in affections of the circulatory and cutaneous system. Accuracy has never been sacrificed to simplicity and students get the definite impression that their clinical studies are only an application of the principles they have learnt in their preclinical course. Each exercise is concise and inferences clear. Most of the experiments are meant as demonstrations to small groups of students and they themselves may be the subjects in many instances. These exercises, therefore, create more interest in the subject and the impressions gained are never forgotten. Many of the exercises detailed in the book deserve to be incorporated in the practical work during preclinical course.

The get-up is excellent. One only wishes that similar exercises for other systems of the human body were written by distinguished contributors in the subject. The book will certainly be very useful to teachers and students alike.

P. D.

PHYSICAL CHEMISTRY OF CELLS AND TISSUES.—

By Rudolf Hober and four Collaborators. 1945. J. and A. Churchill Limited, London. Pp. xiii plus 676. Illustrated. Price, 42s.

THIS book is 'physiology from below'. One wonders how one by-passed so many formidable fortifications, as are presented in its cross sections, and got a glimpse of the top of the subject at all. Most of the fortifications must be castles on the sands and will go the way of earlier castles. Some seventeen years ago, one such castle was glutathione which is not even found in the index of this book.

That five physical chemists should be so mindful of the needs of workers on cells and tissues and yet succeed so little in expressing themselves, mainly because of their weakness for symbols, formulæ, graphs and equations, is amazing.

The narrative even when not encumbered with symbols, formulæ, graphs and equations is far from arresting. 'In many of the synthetic reactions of growth an increase in free energy occurs and such reactions may only occur if they are coupled with an

oxidative reaction furnishing the energy deficit' (p. 425). Thus have the authors enjoyed themselves in writing this book, 'during more than three years of war time'. The workers on cells and tissues, especially of the medical variety, will not be benefited by it.

S. D. S. G.

TEXTBOOK OF BACTERIOLOGY.—By E. O. Jordan, Ph.D., and William Burrows, Ph.D. Fourteenth Edition. 1945. W. B. Saunders Company, Philadelphia. Pp. xvii plus 909. Illustrated

THIS is the 14th edition of this well-known book and in the process of rewriting which was begun in the preceding edition has been continued. The main improvements are that the chapters on yeasts, moulds and actinomycetes have been completely rewritten and incorporated in a longer chapter on medical mycology; the chapter on parasitic protozoa has been replaced by a longer chapter on medical parasitology including the helminths. Most of the illustrations are new. The text pages number 865, index 44 pages. There are 242 illustrations. One of the best textbooks on the subject which the reviewer has seen.

TOPLEY AND WILSON'S PRINCIPLES OF BACTERIOLOGY AND IMMUNITY.—By G. S. Wilson, M.D., F.R.C.P., D.P.H., K.H.P., and A. A. Miles, M.A., F.R.C.P. Third Edition in two volumes. 1946. Edward Arnold and Company, London. Pp. xi plus 970 with xiv index pages and vii plus 1083 with xiv index pages. Illustrated. Price, 60s.

LAST edition of this book had two defects, the bulk was rather large and the type rather small. The first defect has been removed by dividing the book into two volumes, the second remains.

Although the late Topley has been succeeded by Miles the book has retained its original plan. Certain rearrangements, additions and subtractions have been made with consequent improvement.

The book remains a standard English work on bacteriology and immunity. Workers on the subjects will find it indispensable, post-graduate students useful, and physicians who keep abreast with the times helpful. References are ample even for workers in India who, however, are bound to look up more work published in the country on Indian problems.

There is cause for difference of opinion on the prophylactic treatment of rabies. That the treatment is effective was proved by the abrupt drop in mortality from rabies in India, when the strength of the vaccine was increased in 1932.

In view of the economy plan in publishing of books the general get-up is not unsatisfactory. Perhaps a better second impression will be available soon at the same price. No printers' errors attract attention.

S. D. S. G.

TEXTBOOK OF MEDICINE.—By various authors. Edited by J. J. Conybeare, M.C., D.M., F.R.C.P. Seventh Edition. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. xx plus 1164, illustrated. Price, 30s.

FIRST published in 1929 the book is now in its seventh edition. Much of it has been rewritten for this edition and effort has been made to bring it up to date. A new section on sulphonamides has been included, but in view of the rapid progress in knowledge of the use of penicillin it was thought best to omit any detailed description of penicillin therapy.

Seventeen authors on different subjects have contributed to the book. It is of course a matter of immense difficulty to write a textbook of medicine of a little over a thousand pages to cover satisfactorily, even from the students' point of view, the main branches of medicine. Many of the sections have to be so condensed that satisfactory treatment is difficult or impossible. The section on tropical diseases, 38 pages, is not one of the best in the book, but this book is not intended primarily for use in the tropics. The book contains few illustrations.

THE VITAMINS IN MEDICINE.—By Franklin Bicknell, D.M., M.R.C.P., and Frederic Prescott, M.B., Ph.D., A.R.I.C., M.R.C.S. Second Edition. 1946. William Heinemann (Medical Books) Limited, London. Pp. xii plus 916. Illustrated. Price, 50s.

THIS is the second edition of this book, the first edition of which was reviewed in our 1943 volume. The main changes in this edition occur in the chapters on vitamin B complex and riboflavin. These chapters have been largely rewritten and expanded. A short chapter has been added on the essential unsaturated fatty acids and minor fat soluble vitamins. References to original papers now number 4,500. The number of illustrations has been increased from 120 to 280. This book is invaluable to any student of this subject, providing an excellent summary of the known facts and a most excellent guide to the literature of vitamins in medicine.

TEXTBOOK OF OPHTHALMOLOGY.—By Sanford R. Gifford, M.A., M.D., F.A.C.S. Third Edition. 1945. W. B. Saunders Company, Philadelphia. Pp. xviii plus 457, illustrated. Price, 20s.

THIS is a students' textbook which attempts to emphasize the important facts and with little or no emphasis to the unimportant ones. Written and printed in an attractive style with over 200 illustrations and 13 plates, several of them in colour, it presents the subject of ophthalmology in a thoroughly interesting and attractive way. Compared with previous editions the main points are new sections on ptosis, contact glasses, cyclodiathermy and epidemic keratoconjunctivitis.

THE DIAGNOSIS OF NERVOUS DISEASES.—By Sir James Purves Stewart. 1945. Edward Arnold and Company, London. Price, 40s. net

THIS book has now reached its ninth edition since it was first published in 1906. It is stressed in the preface to this edition that the work besides serving as a clinical guide although not a systematic textbook, describes some of the practical methods of approach employed by clinicians in the examination of neurological patients. Starting with a long chapter of 100 pages on physiological anatomy the book proceeds to discuss methods of case taking, delirium, coma, convulsions, involuntary movements, aphasia, and disorders of articulation; brief chapters deal with cranial nerves, pain and abnormal sensations, motor paralysis, inco-ordination, postures and gaits, trophoneurosis, reflexes, affections of the vegetative nervous system, psychoneurosis, electrodiagnosis and prognosis, the cerebrospinal fluid, disorders of sleep and intracranial tumours. The book contains 358 illustrations. It is a well-established book which still holds its own as a textbook on the subject.

A HANDBOOK ON DISEASES OF CHILDREN INCLUDING DIETETICS AND THE COMMON FEVERS.—By Bruce Williamson, M.D. (Edin.), F.R.C.P. (Lond.). Fourth Edition. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 388, illustrated. Price, 12s. 6d.

THIS book is designed mainly for medical students and within its 388 pages it gives an excellent presentation of the subject and a good index. There are 80 illustrations, a few of them in colour, the coloured illustrations showing typical rashes. The text of this edition has been revised and recent advances have been introduced. It is an excellent students' handbook on the subject. Its form is very convenient to handle.

STUDIES IN HYPERTONY AND THE PREVENTION OF DISEASE.—By I. Harris, M.D. 1946. John Wright and Sons Limited, Bristol. Pp. vi plus 114. Illustrated. Price, 12s. 6d.

THIS little book is a record of the author's figures and facts on diet, salts, high blood pressure, morbidity,

clinical efficiency and associated analyses of blood, etc. He has worked with four colleagues.

Although the field of observation is not vast the plan adopted is sound.

One important purpose of the book was to draw attention to the fact that the addition of calcium to the bread in England, as required by the Ministry of Health, was not justified.

S. D. S. G.

ENTOMOLOGY (MEDICAL AND VETERINARY).—

By D. N. Roy, M.D., D.T.M. 1946. Saraswati Library (C18 and 19, College Street Market), Calcutta. Pp. 358. Illustrated. Price, Rs. 25

THIS book satisfies indeed a long-felt want by the D.T.M. students of Calcutta, not that it will not have a very much wider appeal. It has been long overdue, for Alcock's *Entomology for Medical Officers* has not been procurable for years.

Dr. Roy in his prefatory remarks emphasizes that the medical officer is not particularly interested in the morphological study of the insect *qua* morphology, except for its necessity to provide him with a means of identification of any that obtrudes itself in the course of his clinical or health work. Particular attention, rather, is given in the book to the life history of the beasts that cause trouble and ill health. Some means of attacking them is also outlined, though a further work is promised by the author on insecticides, and this should prove very valuable, for the author's esoteric studies at Cambridge have particularly fitted him for such a thesis.

The book in general has been very well arranged, written, and edited. The illustrations are profuse and finely executed. There is a good index and bibliography for each section. Altogether the student is to be congratulated most heartily on the opportunity that has now come his way.

C. S.

CLINICAL BIOCHEMISTRY.—By Abraham Cantarow, M.D., and Max Trumper, Ph.D. Third Edition. 1945. W. B. Saunders Company, Philadelphia. Pp. 647, with 29 illustrations. Price, 32s. 6d. net

THE aim of this book as outlined in the preface is: 'Modern advances in physiology and biochemistry have developed a need, not for another laboratory manual, but for a book designed to correlate established facts with problems encountered daily in internal medicine. The rapidity and magnitude of these developments have resulted in the growth of a highly specialized branch of laboratory medicine, namely, chemical pathology. . . . The aim of this treatise is to consider how the internal environment of the body is altered by certain specific changes in tissue and organ physiology. It is further intended to indicate the manner in which the physician may best avail himself of information which can be obtained by biochemical studies'. To this end the subject of functional diagnosis by chemical methods has been considered in considerable detail. With few exceptions, the technique of laboratory methods has not been discussed, being available in many admirable standard texts on that subject. The book is an extremely careful and thorough publication on the subject. By the omission of much technical detail, the book is rendered very readable. In twenty-five chapters each with a good bibliography all the important aspects of the subject are well covered. The book ends with an extremely good index of seventy pages.

PHYSICAL DIAGNOSIS.—By Ralph H. Major, M.D. Third Edition. 1945. W. B. Saunders Company, Philadelphia. Pp. 444, 437 illustrations. Price, 25s. net

To see, to handle and to read this book is a pleasure. It deals with that branch of medicine which is the basis of the practice of medicine, physical examination.

A preliminary page quotes three sentences from Osler which express the aim and object of the book.

The fifteen chapters are: Introduction; Pain; General inspection; Examination of the head and neck; Examination of the chest; two chapters on the lungs; two on the heart; one each on the pulse, blood pressure, and cardiovascular diseases; the abdomen and genitalia, the extremities and the nervous system each are given a chapter. All these chapters describe clearly and accurately the methods of physical examination, the findings normal and abnormal, and their significance. A final chapter deals with history taking and recording. There are 456 illustrations. A pleasing feature is provided by the notes and illustrations on the history of methods of physical examination. The book is well printed and bound. It can be highly recommended to all medical students and practitioners.

PATHOLOGY OF TROPICAL DISEASES: AN ATLAS.

—By J. E. Ash, Colonel, M.C., U.S.A., and Sophie Spitz, M.D., C.S., A.U.S. 1945. W. B. Saunders Company, Philadelphia and London. Pp. x plus 350, with 941 illustrations, 15 in colour on 257 plates. Price, 40s.

ALTHOUGH a number of texts on tropical diseases are available there is a lack of a comprehensive book dealing solely with their pathology. This is the type of book which would appear to fill this void. The authors being on the staff of the Army Institute of Pathology, Washington, have had access to a wealth of specimens, collected from various sources during the events of past years, an integrated study of which has resulted in the production of this useful atlas. It is divided into twenty-two sections on tropical diseases. Each begins with some epidemiological and clinical notes for orientation and then deals with the pathology followed by a short list of references. The accounts are concise, lucid and up to date. But brevity has certain disadvantages, for instance, a casual reader of the book may conceive the idea that methemoglobin does not appear in the urine in blackwater fever, and that water is not an important means of transmission of amoebic dysentery. There are fine plates of illustrations at the end of each section which include maps, clinical and pathological pictures, photomicrographs and charts of life cycles of parasites. A student of tropical medicine will find these very helpful while studying his text. The book is beautifully produced and is easy on the eyes.

R. N. C.

ESSENTIALS OF DERMATOLOGY.—By Norman Tobias, M.D. Second Edition. J. B. Lippincott Company, Philadelphia and London. Pp. xiv plus 497. Illustrated. Price, 28s.

THIS book is remarkably complete in spite of its small size. Originally offered, in the preface of the first edition, to general practitioners and students it has found acceptance with the entire profession.

Descriptions are of necessity confined to the essentials and may be even inadequate in places (e.g. Leukoderma, p. 362). All the common diseases, including venereal diseases, are, however, fully dealt with. The treatment of all diseases is up to date.

Illustrations though only black and white are excellent and ample, and include a photograph of a case of Cutis hyperplastica. They are part of the narrative and one does not waste time in looking them up.

The nomenclature and index could have been fuller. Gonorrhoea as such is not indexed: Hyperkeratosis blennorrhagica is Keratoderma blennorrhagicum: the dermatosis of the palm is Keratoderma palmaris but that of the subungual area Hyperkeratosis subungual.

The paper, printing and binding are good. Only one error has arrested the reviewer's attention: Hyperkeratosis subungual is on page 425, not on 424 as shown in the index.

The book is easily one of the best of its size.

S. D. S. G.

BOOKS RECEIVED

1. Nutrition. Bulletin No. 18. June, 1946. Published by the Department of Food, Government of India, New Delhi. Pp. 25. Illustrated. Price, 4 annas.
2. Annual Report of the Sri Ramakrishna Math Charitable Dispensary, Mylapore, Madras, for the year 1945. Issued by the President, Sri Ramakrishna Math and Mission, Brodie's Road, Mylapore, Madras.
3. Studies on Protein, Fat and Mineral Metabolism in Indians. By K. P. Basu, D.Sc., Ph.D. Special Report No. 15 of the Indian Research Fund Association. Published by the Indian Research Fund Association, New Delhi. Pp. 64. Price, 12 annas only.

Abstracts from Reports

REPORT OF THE KASHMIR MEDICAL MISSION OF THE CHURCH MISSIONARY SOCIETY FOR THE YEAR 1945

DURING the year there was shortage of staff which influenced the output of work, both in quantity and quality. There were 16,865 new out-patients, and their total attendances were 41,203. The in-patients numbered 2,247 of whom 1,627 were males and 620 females. Four thousand three hundred and eighty surgical operations were performed. The other works included laboratory investigations, x-ray examinations and sale of gospels. The report contains a statement of income and expenditure for the year 1945 together with a list of donations, subscriptions and offertories which amount to nearly Rs. 14,000. All who are interested in the work may send their subscriptions or donations to the Mission.

Correspondence

TRANSMISSION OF KALA-AZAR*

SIR,—In your issue of October 1944 you were kind enough to publish a paper written by Malone and Brooks on the transmission of kala-azar.

In that paper we argued that *Phlebotomus argentipes* had not been proved the natural vector of kala-azar: that there was very strong epidemiological evidence against the sandfly transmission theory: that what was known of the bionomics of *P. argentipes* in nature seemed to preclude it from being the vector of kala-azar or any other disease: that no argument based on analogy with oriental sore was valid as it has not yet been proved that sandflies convey oriental sore in nature: and that the highly successful transmission experiments of Swaminath, Shortt and Anderson (*Ind. Jour. Med. Res.*, 30, 1942) were carried out under conditions so artificial that they afforded no proof that the fly was the actual vector under natural conditions.

None of the statements of fact quoted by us have been questioned and none of our arguments have been refuted, yet it is still definitely asserted that it has now been finally proved that *P. argentipes* is the natural vector of kala-azar.

We have seen only one reference to our paper, apart from correspondence in your journal. At an ordinary meeting of The Royal Society of Tropical Medicine and Hygiene (*Trans. Roy. Soc. Trop. Med. and Hyg.*, 39, 1, 1945, page 23) Colonel Shortt dismissed our arguments in the following words: 'In a recent issue of the *Indian Medical Gazette* Malone and Brooks (1944) have brought up the question of transmission of kala-azar by the sandfly once more. . . . It is curious that these two workers, who so far as I know have never done any work themselves on the transmission of kala-azar, should attempt a destructive criticism of all the work done by others . . . in fact they lay themselves open to a complete refutation of their assertions,

* By a coincidence an article by Colonel Shortt on the subject has also been received. It appears on page 310.

were one inclined to initiate a contest in polemics. This is neither the time nor the place to indulge in this recreation.'

It is now a year since the above statement was made and I greatly fear that it is the intention of the supporters of the sandfly transmission theory to ignore our arguments in the hope that those arguments will soon be forgotten.

In the interests of Science I would suggest that the time for this 'complete refutation' has come and that the columns of your esteemed journal would be as suitable a place for it as any.

I can assure you, Sir, that for our part there will be no contest in polemics.

R. H. MALONE,

LIEUTENANT-COLONEL, I.M.S. (Retd.).

KASAUJI.

PHARMACY BILL

SIR,—I have the honour to forward the following:—

While welcoming the introduction of a bill to regulate the profession of pharmacy the Pharmaceutical Society of India would like to make the following suggestions for implementing the objects of the Pharmacy Bill.

(1) In nominating members to the central as well as the provincial Pharmacy Council no provision has been made for a representative of the Pharmaceutical Society of India on either of these boards though this society has been in existence since 1925 and has been doing yeoman service in bringing about the present bill. This fact has been recognized by the Government of Madras.

(2) The society wishes to bring to the notice of the government that while members of the teaching and medical profession have representatives on the board, members who are actively engaged in the profession of pharmacy, viz; in management and running of pharmacies and dispensaries, have been left out, making the councils purely academic and not practical. The society therefore suggests that in both the pharmaceutical councils, central as well as the provincial, the nomination by the Central or the Provincial Government as per chapter II, clause (b), and chapter III, clause (b), the three persons mentioned therein having a degree or diploma in pharmacy should also be actively engaged in the business or profession of pharmacy.

(3) Again in chapter I, clause 7, and chapter III, clause 23, the society is of opinion that the term of office of the president may be three years and of other members four years as otherwise it may be either too long or too short. The president and some of the members may remain for three years and others for four years.

(4) Chapter IV, clause 31. As regards the qualifications for entry on the first register the society would like the wording of the clause (9) to be more clear, viz, 'holds a degree or diploma in pharmacy or pharmaceutical chemistry of a British India university or a diploma in pharmacy granted by an authority in British India.'

(5) Chapter IV, clause 34, renewal fees. The Pharmaceutical Society of India is of opinion that this clause must be completely deleted as this is not a licence fee which has to be renewed every year. A person once registered as a pharmacist should be registered for life. This must be followed in the lines of registered graduates or registered medical practitioners.

In conclusion this association wishes to bring to your notice of its status and standing. It has as its members only qualified pharmacists and is established and registered under Companies Act during 1925. It has helped a good lot the Drugs Advisory Committee that started early in 1929 to formulate these acts. This association is recognized by the Government of Madras as well as the Pharmaceutical Society of Great Britain. It is running in the same lines and methods as the Pharmaceutical Society of Great Britain.

The Pharmaceutical Society of India is the only pharmaceutical organization who have the privilege of becoming members of the International Pharmaceutical

Federation. Copy of the letter from the Secretary, The Pharmaceutical Society of Great Britain, is herein appended for your information.

Yours faithfully,
A. LAZARUS,
Secretary,
Pharmaceutical Society of India.

(True Copy)

THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN

PATRON : HIS MAJESTY THE KING
17, Bloomsbury Square, London
28th March, 1946

JCT/HNL.

DEAR MR. LAZARUS,

We have been doing our best to revive the International Pharmaceutical Federation, which was doing excellent work before the war in promoting professional friendship between pharmacists of different countries. The President, Dr. Madsen of Copenhagen, and the Secretary, Dr. Potjewijd of Winschoten, Holland, are both alive and well and have resumed their offices, and most of the funds (I think some two or three thousand Dutch florins altogether) were saved from the Germans.

We held a meeting of the Executive Committee in London at the end of last year, which four members managed to attend, and we made provisional plans for a further meeting probably next year. We do not feel that we can call a general assembly by reason of travel difficulties.

At the recent meeting I was invited to act as one of the vice-presidents pending confirmation at a meeting of the assembly, and I was asked particularly to do what I could to arouse the interest of English-speaking pharmaceutical societies in the Federation. I am accordingly writing to invite the Pharmaceutical Society of India to join the Federation. It would be a great encouragement to the Federation in these difficult days of reconstruction.

Subscriptions to the Federation are calculated on the basis of 50 Dutch florins per delegate, and the number of delegates to which an association is entitled is:—

Associations having a membership of—

less than 500	1 delegate
500-1,000	2 delegates
1,000-1,500	3 "
1,500-2,500	4 "
2,500-5,000	6 "
more than 5,000	8 "

The Secretary's address is: Dr. T. Potjewijd, Winschoten, 9c Boschplein, Holland. If, as I hope, your society can see its way to join, will you kindly send to Dr. Potjewijd the following information: the names and addresses of the President and Secretary, the names of persons who could be regarded provisionally as delegates in the event of an assembly being arranged (although obviously in present circumstances there could be no obligation upon them to attend) and if possible the subscription for the year 1946.

Yours sincerely,
(Sd.) HUGH N. LINSTED, O.B.E.

PHARMACY BILL

SIR,—Your circular letter dated 29th April mysteriously reached me just the other day and I hasten to reply.

In the light of the preamble adumbrated in the opening sentences of the Bill, the word 'Pharmacist' envisages two types: (1) the scientifically trained person with a knowledge of a branch of chemistry involved in the manufacture of potent therapeutic substances and (2) the person who is skilled in dispensing with just a working knowledge of the action

dose and use of the therapeutic substances. The former may not be skilled in the requirements of the latter and vice versa. The Bill therefore does not clearly categorize the different zones of activity of the two groups.

Again in chapter IV, section 31, qualifications are specified for entry on first and subsequent registers in (1), (2), (3) and (4). In all the above classes except (1) the main qualification is knowledge of the art-cum-science of dispensing prescriptions. One feels that class (1) should also have knowledge of dispensing. A medical graduate is also prescribed this training in dispensing which forms part of his university examination. It is therefore suggested that either there be two categories in the register of pharmacists, i.e. (1) the industrial or manufacturing pharmaceutical chemist and (2) the dispensing chemist whose basic knowledge is of an inferior grade or that the industrial or manufacturing chemist who is the holder of a degree in pharmaceutical chemistry be given the facility to apply his scientific knowledge to the art-cum-science of dispensing. A practical course in a dispensary should be insisted.

Some provision must be made for raising the standard of the dispenser or compounder to bring him into line with the holder of the Diploma of Pharmacy.

The 'high-browed' manufacturing chemist unfortunately in some quarters seems to feel that the medical man is too interfering and dictatorial. Does he realize that the profession of pharmacy primarily exists to cater to the needs of a medical man and that therefore the medical man is perfectly within his bounds in expecting from or insisting on, or dictating to, the pharmacist? Let him turn back and have a glance at the attitude of Bertheim the chemist working in Paul Ehrlich's laboratory at the time of the production of '606'. Ehrlich was not much of a chemist but he passed his ideas '... atoxyl can be changed. Now my dear Bertheim, we can change it into a hundred, a thousand new compounds of arsenic. ...' A medical man's interest in the profession of pharmacy is a most natural thing. Arguments when they reach a stage of denouncing that interest in the words '... people (meaning medical men and pharmacologists) who should have nothing to do with it (the Pharmacy Bill) are opposing it' reveal that something is rotten in the state of ...

In view therefore of the scope of the Bill it is expedient for the degree-holder in pharmaceutical chemistry, before he is entitled to get himself registered, to have a short course or practical training in an approved dispensary. If an analogy is warranted, it is that of a civilian official who during his probation has to learn a work of a kind from the village official (the Karnam) or the police official from the traffic constable in street crossings.

ANDHRA MEDICAL COLLEGE,
VIZAGAPATAM.

V. ISWARIAH,
B.A., M.B., M.R.C.P.

PHARMACY BILL

SIR,—I fail to understand the urgency of the Pharmacy Bill published in the February issue of the *Indian Medical Gazette*, its main object, as stated in the resolution, is to eradicate the danger of compounding and dispensing medicines by unqualified persons. Its aim, no doubt, seems to be a laudable one but I have every doubt if its object will ever be fulfilled in the practical field even if we have so many high sounding councils all over the country, as we have the sad experiences of observing how the provincial State Medical Faculties (at least I can speak of my own provincial Faculty) safeguard the interests of the public, as well as the medical practitioners, by doing nothing so far to remove quackery which is none the less dangerous than the unqualified dispensers and compounders.

I firmly believe the profession of pharmacy is certainly not going to be a bit improved or benefited by

this Bill and it would be desirable if the sponsors of the Bill have the good sense to drop it altogether.

If it at all be passed, it will prove to be only a burden on the present and future pharmacists in the shape of registration fees and annual renewal fees till their demise or their leaving the profession.

If there be any defects in the existing pharmaceutical courses—the provincial State Medical Faculties can take up this matter in their hands and on due enquiry and inspection—these can be rectified and improved.

And for the maintenance of the register—there is one such in our province which keeps a record of all the qualified compounders.

Pray—where is its urgency then?

R. CHATTERJEE, M.B.

SHREE VISHUDHANAND SARASWATI
DATAVYA AUSADHALAYA,
37, BURTOLLA STREET,
BARABAZAR, CALCUTTA.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL E. T. N. TAYLOR, C.I.E., Additional Deputy Director-General, Indian Medical Service (Personnel), was appointed to officiate as Deputy Director-General, Indian Medical Service, in addition to his own duties, during the absence of Colonel A. K. Sahibzada, O.B.E., granted leave.

Major A. H. Mallick, I.M.S./I.A.M.C., assumed charge of the post of Assistant to the Senior Medical Officer in the Medical Department of the Andaman and Nicobar Islands on 11th September, 1945.

Captain E. E. Lefevre, I.M.S./I.A.M.C., assumed charge of the post of Medical Officer in the Medical Department of the Andaman and Nicobar Islands on 16th September, 1945.

Major C. L. Greening, an officer of the Research Department, is appointed Assistant Director, Central Research Institute, Kasauli, with effect from 6th December, 1945.

The services of Major J. R. Dogra, an officer of the Medical Research Department, are placed temporarily at the disposal of the Government of Bombay for appointment as Assistant Director, Haffkine Institute, Bombay, with effect from the 6th January, 1946.

Major P. M. Kaul is appointed Additional Deputy Public Health Commissioner with the Government of India (Epidemics and Communicable Diseases), with effect from the 26th January, 1946.

The Secretary of State for India has sanctioned the permanent reversion to military employment of Major J. W. Bowdan, an officer of the Bihar Indian Medical Service Cadre, with effect from the 14th February, 1946.

Lieutenant-Colonel S. Annaswami is appointed to be the Superintendent of Alipore Central Jail, with effect from the 25th February, 1946, until further orders, *vice* Lieutenant-Colonel M. Das, M.C., I.M.S. (retired).

Major A. T. Andreason is appointed to be Professor of Surgery, Medical College, Calcutta, with effect from the 10th March, 1946, *vice* Lieutenant-Colonel F. J. Anderson, C.I.E., I.M.S. (retired).

Major G. Milne, an Agency Surgeon, on return from leave, resumed charge of his duties as Agency Surgeon, Bundelkhand, with effect from the afternoon of the 24th March, 1946.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service with the R.I.N.V.R.:—

Captain G. V. Rao. Dated 1st November, 1945.

The undermentioned officers of the I.M.S. (E.C.) revert from the R.I.N.V.R., and are seconded to the I.A.M.C.:—

Surgeon Lieutenant K. Parthasarathy. Dated 23rd September, 1945.

Captain Miss A. F. Hankins, I.M.S./I.A.M.C., assumed charge of the Post Officer-in-charge Women's Hospital in the Medical Department of the Andaman and Nicobar Islands on 24th September, 1945.

Surgeon Lieutenant R. Tyagarajan. Dated 19th October, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

Mohammed Nazir. Dated 10th November, 1945.

Amiya Ranjan Ray. Dated 12th November, 1945.

Vasant Anant Awalegaonkar. Dated 2nd December, 1945.

Manibhai Dahyabhai Desai. Dated 3rd December, 1945.

LEAVE

Lieutenant-Colonel F. H. Whyte is granted an extension of leave *ex-India* for 6 months on medical certificate, the first 2 months on average pay and the balance on half average pay, with effect from the 10th March, 1946.

In partial modification of this Department Notification No. F.9-56(4)/45-H, dated the 14th March, 1946, Lieutenant-General Sir J. B. Hance, K.C.I.E., O.B.E., K.H.S., Director-General, Indian Medical Service, is granted leave preparatory to retirement *ex-India* on average pay for 6 months and 22 days, combined with leave on half average pay for 1 month and 8 days, with effect from the afternoon of the 11th March, 1946.

PROMOTIONS

The undermentioned officer is granted the local rank of Colonel without effect on pay and pension, whilst employed as Inspector-General of Civil Hospitals, C. P. and Berar:—

Lieutenant-Colonel L. K. Ledger, O.B.E., I.M.S. Dated 12th November, 1945.

The undermentioned Indian Medical Service Officer is advanced to the List of Special Selected Lieutenant-Colonels:—

Lieutenant-Colonel C. M. Nicol, C.I.E. Dated 5th December, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
(Emergency Commissions)

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Captains to be Majors

F. T. Harrington. Dated 31st October, 1945.

D. D. Boovariwala. Dated 12th November, 1945.

T. J. Davies. Dated 22nd December, 1945.

2nd January, 1946

K. Rajamannar.

A. H. Khan.

H. Khan.

M. P. N. Nambiar.

K. B. Taneja.

H. R. Nischol. Dated 5th January, 1946.

A. D. Wilson. Dated 7th January, 1946.

C. R. Krishnaswami. Dated 9th January, 1946.

R. M. Gilchrist. Dated 10th January, 1946.

15th January, 1946

B. Singh.

N. Krishnaswami.

M. A. Nair.

J. L. G. Pinto. Dated 20th January, 1946.

K. S. Ramaswami. Dated 21st January, 1946.

26th January, 1946

S. V. Kail.

A. A. Khan.

V. R. Thayumanswami. Dated 29th January, 1946.

The undermentioned officer is confirmed to the rank of Lieutenant from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

J. R. Pereira. Dated 7th August, 1942.

INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commissions)
 (WOMEN'S BRANCH)
Captains to be Majors

Mrs. I. L. H. Hewlett. Dated 29th November, 1945.
 Miss M. K. Beattie. Dated 1st January, 1946.

RELINQUISHMENTS

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Lieutenant-Colonel :—

INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commission)—*Specialist*

Ty. Lieutenant-Colonel R. Nagendran. Dated 7th March, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Lieutenant-Colonel M. V. Ramanamurti, F.R.C.S. (Edin.), 26th January, 1946, and is granted the honorary rank of Lieutenant-Colonel.

Captain B. B. Mandal, 27th January, 1946, and is granted the honorary rank of Captain.

Ty. Lieutenant-Colonel G. V. S. Murthi, 28th February, 1946, and is granted the honorary rank of Lieutenant-Colonel.

The undermentioned officers are permitted to relinquish their commissions on release from army service, and are granted the honorary rank of Majors :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Major E. G. Michelson. Dated 20th January, 1946.

(Emergency Commissions)

Major Satyendra Nath Basu. Dated 17th February, 1946.

Captain (T./Maj.) M. S. Kapur. Dated 28th February, 1946.

Major S. N. Chatterjee. Dated 4th March, 1946.

(Specialist)

Kalipada Banerjee. Dated 16th March, 1946.

The undermentioned officers are permitted to relinquish their commissions on reversion to the Indian State Forces :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain Ghulam Nabi. Dated 30th January, 1946.

Captain C. G. Muller, 5th February, 1946, on grounds of ill health and is granted the honorary rank of Captain.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captains :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain G. A. Sundaram. Dated 27th February, 1946.

Captain P. R. R. Menon. Dated 2nd March, 1946.

Captain N. J. Rao. Dated 8th March, 1946.

(WOMEN'S BRANCH)

Captain (Mrs.) E. M. McDonald. Dated 31st January, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captains :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain D. R. Shirhatti. Dated 6th February, 1946.
 Captain S. P. Notani. Dated 14th February, 1946.

The undermentioned officers are permitted to relinquish their commissions on grounds of ill health :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

F. D'Souza, 19th December, 1945, and is granted the honorary rank of Lieutenant.

Captain M. Sen, 23rd February, 1946, and is granted the honorary rank of Captain.

INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

Captain (Miss) Perin Hamidullah, 18th January, 1946, and is granted the honorary rank of Captain.

Major (Miss) E. H. Smith, 5th February, 1946, and is granted the honorary rank of Major.

(WOMEN'S WING)—*Indian*

Captain (Mrs.) Una Wickens, 7th January, 1946, and is granted the honorary rank of Captain.

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Original Articles

CAUSALGIA

A REPORT ON 32 CASES

By H. R. PASRICHA

LIEUTENANT-COLONEL, I.M.S.

SINCE Mitchell *et al.* described causalgia in 1864, the opportunities to study this condition in detail have not been many. The following report is based on a series of 32 cases which came under my care during 1944 and early part of 1945. After March 1945 no cases were received up to the end of the year, a very important fact. As I shall explain later this can be definitely correlated with the general use of penicillin in forward areas. It is more than likely that infection in wounds of the nerves plays a very important part in the ætiology of causalgia.

All these cases were soldiers who had been wounded on the various battle-fields during the period mentioned above. Out of 32 cases 18 were Gurkhas, a preponderance which cannot be easily explained by assuming a larger number of Gurkha troops employed. For quite a long time it was not possible to offer any explanation for this increased liability of Gurkhas to this disorder. Later it was realized that Gurkhas as a race had a marked tendency to excessive scarring and keloid formation. A cœhsus of all the Gurkha patients suffering from all varieties of wounds revealed that out of 95 cases 38 showed a well-marked evidence of keloid, an incidence far exceeding any seen in Indian troops. The preponderance of causalgia in Gurkhas may be explained by assuming that just as they are more liable to form keloids so they are more likely to develop excessive intra-neural fibrosis. Support is lent to this view by the fact that the use of penicillin, since it reduced infection, reduced intra-neural scarring also. This is the reason why cases of causalgia stopped coming to this centre after a general use of penicillin in the forward areas.

Incidence

In a series of 1,390 cases of peripheral nerve injury 32 (2 per cent) had causalgia. It is rather a high percentage, but may be explained partly by the fact that some of the nerve cases were treated elsewhere, whereas most of the cases of causalgia were sent to us. Their distribution was as follows :—

Nerve involved	Number of cases
Median	19
Ulnar	1
Tibial	12
TOTAL	32

Types of missiles	Number of cases
Gun-shot wounds	16
Shell or bomb splinters	6
Grenade wounds	10
TOTAL	32

SITE OF INJURY	
Upper extremity	Cases
Neck ..	3
Shoulder ..	3
Axilla ..	1
Arm ..	10
Forearm ..	2
Hand ..	1
TOTAL ..	20
Lower extremity	Cases
Buttock ..	3
Thigh ..	6
Leg ..	2
Multiple ..	1
TOTAL ..	12

Age incidence.—All the patients were young men between the ages of 19 and 40, the average being 24. The numbers in accordance to decades are as follows :—

	Cases
11 to 20	5
21 to 30	24
31 to 40	3
TOTAL	32

Associated Lesions

Compound fractures.—There were four cases with compound fractures: radial 1; ulnar 1; humerus and ulnar 1; clavicle 1.

Associated nerve lesions :—

	Cases
All branches of the brachial plexus ..	4
Radial nerve	1
Median nerve	4
Ulnar nerve	4
Median and ulnar nerves	3
Sciatic nerve	9
Tibial nerve	2
Peroneal nerve	1
No nerve damage was detected clinically in ..	4
TOTAL	32

This shows that although 19 cases were of median causalgia, only four revealed clinical evidence of damage to the median nerve alone. In another seven, the damage to other nerves was associated with damage to the median nerve. Four cases showed no signs, motor or sensory, suggesting any injury to any of the nerves of that limb. This would justify a conclusion that causalgic pain may arise even though the nerve is conducting fully its motor and sensory functions. In other words causalgia may be produced by a nerve lesion which interferes with neither the somatic sensory fibres nor the motor fibres.

An analysis of the sensory findings associated with causalgia showed that in seven cases there was complete loss of pain and tactile sensation in the area to which the patient referred his

pain. This would suggest that complete damage to the somatic sensory fibres may not prevent the onset of causalgic pain. Support is lent to this view by the results of some of the methods of treatment adopted for the relief of pain in this condition. Sicard's (1916) method of injection of alcohol or Smithwick and White's (1935) modification of crushing the peripheral nerves above the ankle may be employed. Foot can be rendered insensitive in this way. Smithwick and White are frank enough to admit that these methods frequently failed to relieve the pain. They go on to add, 'Why interruption of all known sensory fibres should fail and be followed by pain in an insensitive area, is not known.'

Vascular damage.—In five cases the damage to the main blood vessel of the limb was associated. Ligation of the vessel of the limb preceded the onset of the pain by a few days. Three cases involved damage to axillary artery; one to brachial and one to posterior tibial. If ischæmia is a cause of causalgia, as it is alleged, then it did not play an important part in this series of cases since there was evidence of damage to vessel only in a small number of cases.

Symptoms and Signs

Mitchell *et al.* (1864) first described causalgia in soldiers following penetrating wounds involving the nerves. They described it as hyperæsthesia of the hand or foot following an injury in the region of a peripheral nerve. The main features of this disorder may be grouped as follows: 1. Burning pain and disturbance of sensation. 2. Vasomotor changes. 3. Trophic disturbances.

1. *Pain and sensory disturbances.*—The time of onset of pain is very important; it invariably follows the injury within a few days. There is no doubt that several conditions can give rise to burning pain of varying intensity which are not well understood. But in cases where injury to a nerve has resulted in a transient loss of conduction (neurapraxia) during the recovery stage the patients sometimes complain of burning pain very much like causalgia which is probably a part of protopathic pain of head. In all such cases the onset of pain is much later, the interval between the injury and occurrence of pain extending to several months.

The three classical characters of pain described by Mitchell *et al.* still constitute the best description of pain. The pain is burning, spontaneous and constant. It is liable to exacerbations on the slightest physical or emotional stimulus. The patient is never free of pain. His hand or foot is on 'fire'. The pain is always worse during the day but improves during the night. The patient is afraid of exposing his hand or foot to the sun. Very rarely, some of them (two in this series) preferred to wrap up the part. If the pain is

severe, the patient derives great relief by soaking the affected part in water. The intensity of pain is variable from trivial burning sensation to a state of torture. In a very marked case the patient is afraid of exposing his limb to draught; he resents noises close to him and is afraid even to talk or eat. In trying to engage some of the severe cases in talk, it was noticed that they insisted on soaking their hands in cold water before answering a question although the hand was already wrapped up in a piece of wet cloth.

In this series the pain was classified as trivial if it did not prevent the patient from engaging in normal activities in the hospital. In moderately severe group, the pain disturbed him considerably during the day preventing him from engaging in normal activities, but it did not disturb his sleep at night. In the severe group, the patient could not sleep at night. In the very severe group, the patient was very miserable, sleepless, unable to eat and with all the features of pain well marked. The numbers according to the classification were trivial 8, moderately severe 2, severe 8, and very severe 5.

Hyperæsthesia in the causalgic area was present only in nine cases, being marked in five. In all cases showing hyperæsthesia, the sensations in the area were intact. Conversely, cases with anæsthesia of the causalgic area did not, at any time, show hyperæsthesia.

2. *Vasomotor changes.*—Hyperidrosis. There was evidence of excessive sweating in nine cases (28 per cent). Four were very severe cases. Of the remaining 23 patients, in two the hands were excessively dry and rough although they were suffering from severe causalgic pain. Excessive sweating, therefore, is not a constant feature. This is what one would expect. Since hyperidrosis is due to irritation of the sudomotor fibres in the nerves, its incidence is bound to vary according to the degree of involvement of the sudomotor fibres and whether the nerve is completely divided or not. A lesion causing interruption of a large number of sudomotor fibres would obviously not cause excessive sweating but hypo- or anhidrosis.

Changes in circulation.—These changes, caused by involvement of the vasomotor fibres in a nerve, do not seem to bear a constant relationship to causalgia. Sometimes the affected limbs show signs of loss of vasomotor tone in the part distal to the lesion. The limb in such cases gets congested on hanging and blanches on elevation. More often there is no evidence of loss of vasomotor tone. The affected hand or foot tends to be paler and colder than its fellow and does not show any marked change on change of posture.

3. *Trophic disturbances.*—In cases of long standing the skin tends to atrophy. It is thin, dry and glossy, and the nails tend to get thickened and brittle. Only one patient of this series showed these changes. He had had

severe causalgia for five months before coming for treatment.

Differential Diagnosis

As already stated there is little doubt that pain of burning character can arise from causes other than causalgia. One example is the pain that occurs during the recovery stage of a nerve in which transient interruption of function has resulted from injury. In this series, before a pain was classified as causalgic, it had to be (a) in the region of a peripheral nerve subjected to damage, (b) spontaneous, (c) continuous, (d) liable to exacerbations, and (e) burning in character. The time of onset was considered very important. Causalgic pain follows injuries within seven to ten days or at the most a fortnight to three weeks. Any pain that took longer was looked upon with suspicion. This was done in order to exclude cases of protopathic pain. With this object in view all cases showing evidence of recovering function were not classified as causalgic. The cases where there was no evidence of sensory or motor interruption at the time of examination were assumed to have had transient sensory or motor changes which had been missed during the patient's journey down to us from the front line.

The line of treatment adopted depended upon the severity of the pain. Although Mitchell was of the opinion that causalgia was a self-limiting disease, our experience was different. If the pain was at all severe it resulted in profound changes in the mental condition of the patient. No attempt was made to allow severe causalgia to subside spontaneously, but trivial and moderately severe cases were allowed to subside by themselves. If the patient complained of pain interfering with his activities or sleep treatment was given. The first step always was to inject 1 per cent novocaine solution around the sympathetic trunk at the appropriate level—upper dorsal in arm cases and upper lumbar in leg cases. If the patient showed a good response and the pain was not severe, an attempt was made to see if the pain would subside on repeated injections. In some cases it did. Where the pain was severe the injection gave us a clue to the success or otherwise of surgical treatment. Where the response to injection was good and pain was relieved for sometime, treatment was undertaken with considerable assurance that the patient would benefit from it.

In this series the pain subsided spontaneously in four cases and yielded to repeated injections in four cases, while sympathectomy was done in 21 cases and periarterial sympathectomy in three.

Periarterial sympathectomy was undertaken as an experiment. Leriche in 1913 first reported relief of causalgic pain by this procedure. The present attempt was not an effort to confirm his findings but to enlarge upon them. The results were quite interesting. In two cases the

posterior tibial artery behind the medial malleolus and in one case the radial artery just above the wrist were exposed under local anaesthesia taking good care that novocaine did not extend deeper than the deep fascia. In other words, an attempt was made to explore the perivascular sympathetics without interfering with their conduction. The arteries were denuded of the fibres surrounding them. The patient complained of the pain deep down in the foot or hand on interference with these fibres. The pain elicited was severe but vague and diffuse. It was in the foot or hand and deep down in the bones. Lastly, it was found that there was little or no pain on stimulating the fibres with rapid faradic current, but pain of the type described above was elicited on crushing the fibres. Apparently, dragging and crushing were the two effective stimuli with these nerve fibres. All the three cases were of moderately severe pain only and had no pain after perivascular sympathectomy. They have remained free of pain for four months and are still under observation. This would justify the conclusion that some of the afferent sympathetic fibres course to the destinations in skin and other peripheral *via* the vessels. These fibres are probably not really sympathetic but ordinary somatic fibres travelling with sympathetic fibres.

Lumbar sympathectomy was done in five cases. The approach was through an oblique incision in the flank and the trunk was exposed extraperitoneally. The second and third lumbar ganglia with the intervening trunk were removed. This was found quite effective in relieving the pain completely, although it is agreed that this does not completely denervate the entire leg. In a certain number of cases the fourth ganglion was also removed but this presented no advantage over the less complete operation. Dorsal sympathectomy was done in 16 cases, 14 being anterior operations (Leriche, 1913). In these cases the lower cervical and upper dorsal ganglia were exposed through an incision in the lower part of the neck. The clavicular head of the sternomastoid was cut and the scalenus anterior was divided near its insertion. The chain was then exposed by mobilizing the subclavian artery and pushing it down. The other two were posterior route (Adson) operations. One of these was performed by my colleague Major A. J. Slassor. My preference was for the anterior operation, because it was neater and easier and less damaging than the posterior, since it did not involve resection of ribs or cutting of big muscles. It was urged several times that an adequate exposure of the trunk was not possible through the anterior route. It was particularly pointed out that it was difficult to go down as far as the third dorsal ganglion through the anterior route. That was not my experience. In every case I found it quite easy to expose the trunk up to and just below the level

of the third dorsal ganglion. This was confirmed in left-side operations by going down as far as the arch of the aorta. The only time I had difficulty in exposing the trunk was in a case where the patient had a big bony mass around the middle of the clavicle as a result of previous fracture. In one case in which the posterior operation was adopted the choice was forced by the fact that the patient had had his subclavian artery exposed already by another surgeon in an attempt to control bleeding.

The operation in all cases consisted of division of the sympathetic trunk below the level of the third dorsal ganglion and resection of the second and third rami. The divided trunk was then turned up and stitched away from its normal situation to prevent regeneration (Telford). This did not result in a Horner's syndrome.

The individual results of the cases are given with the case summaries. In general the results in all cases were dramatic. As soon as the patient came round he was free of pain and remained free of pain subsequently. In one case only, a certain amount of hyperæsthesia persisted. The patient, however, maintained that he was much better after the operation in so far as the burning pain had disappeared. The hyperæsthesia persisted for about three months and then slowly disappeared. This was a very severe case of five months' duration. Twelve out of these 21 cases have been discharged. On an average, they remained under observation for three and a half months after operation, the shortest period being one month and the longest eight months. Nine cases are still under observation for a period varying from four to ten months after operation. All the cases are still free of pain.

Case Reports

1. *Case 6.*—Median causalgia. Machine-gun wound, right arm, on 26th April, 1944. Severe burning pain in right hand seven days after injury. Typical causalgic pain. Severe case. No paralysis. Sensation intact in causalgic areas. Hyperæsthesia present. Injection of stellate ganglion on 29th July, 1944. Relief of pain for three hours. Injection repeated on 1st August, 1944. Short-lived relief. Chain divided on 25th August, 1944. Complete relief. Discharged on 1st August, 1945.

2. *Case 7.*—Median causalgia. Gun-shot wound, left arm, on 24th July, 1944. Severe burning pain started five days after injury. No notes of initial sensory findings. On 13th October, 1944, pin-prick and touch sensations present in the causalgic area, but dull. No hyperæsthesia. No paralysis. Chain injected with novocaine on 23rd October, 1944. Pain relieved for short time. Injection repeated on 6th November, 1944. Typical Horner's syndrome. Relief of pain. Chain divided on 15th November, 1944. Complete relief. Discharged on 18th January, 1945.

3. *Case 13.*—Median causalgia. Multiple grenade wounds, left palm, on 27th May, 1944. X-ray revealed three metallic foreign bodies; one in the vicinity of median nerve in the palm at the base of thenar eminence. Very severe pain with marked hyperæsthesia. No loss of sensation. Paralysis of thenar muscles only. Duration five months. Chain injected on 15th October,

1944. Relief for a very short time. Chain divided on 18th October, 1944. Relief of burning pain after operation but hyperæsthesia persisted for three months. Discharged on 17th February, 1945.

4. *Case 18.*—Median causalgia. Grenade wound, right shoulder, on 12th June, 1944. Severe causalgic pain in palm of right hand. Started eight days after injury; very severe. Dulling of pin-prick and touch in the causalgic area. No hyperæsthesia. No initial sensory findings. Paralysis of all median muscles except pronator teres, flexor or carpi radialis, and palmaris longus. Injection on 18th August, 1944, with short relief. Operation on 20th August, 1944. Chain divided. Complete relief. Discharged on 14th April, 1945.

5. *Case 21.*—Median causalgia. Gun-shot wound, neck, left. X-ray shows fracture of lateral masses of 6th and 7th cervical vertebrae and small metallic foreign body. Had complete flaccid paralysis of left arm and paralysis with marked exaggeration of all reflexes of left leg. No sphincteric trouble. Typical causalgic pain eleven days after injury in palm of left hand. Injection of chain on 10th March, 1945, with short relief. Chain divided on 21st March, 1945. Neurolysis of roots of the brachial plexus through the same incision at the same time. Complete relief of pain and almost complete recovery of arm muscles. No anaesthesia on causalgic area. Discharged on 2nd November, 1945.

6. *Case 33.*—Tibial causalgia. Gun-shot wound, left thigh, on 30th March, 1945. Moderately severe. Causalgic pain in sole of left foot. Paralysis of all leg muscles except biceps semitend. and semimemb. Injection of lumbar chain on 14th May, 1945. Marked relief. Foot congested, dry and warmer than its fellow. Periarterial sympathectomy of the posterior tibial artery behind the medial malleolus on 20th May, 1945. Complete relief. Discharged on 24th September, 1945.

7. *Case 24.*—Tibial causalgia. Gun-shot wound, left thigh, on 30th March, 1945. Severe causalgic pain in the sole of left foot. Started seven days after injury. Paralysis of leg muscles the same as in the above case. Complete loss of sensation in sole of foot. Injection on 11th April, 1945. Short relief. Chain divided on 16th April, 1945. Complete relief. Under observation.

8. *Case 31.*—Tibial causalgia. Multiple gun-shot wound, left elbow and both buttocks, on 23rd November, 1944. Severe causalgic pain in sole of left foot started four days after injury. Paralysis of tibial muscles. Complete loss of sensation in sole of foot. Injection of lumbar chain on 3rd April, 1945. Chain divided on 11th April, 1945. Complete relief. Discharged on 7th August, 1945.

9. *Case 30.*—Tibial causalgia. Shell wound, left buttock, on 8th November, 1944. Moderately severe causalgic pain came on three days after injury. Exploration of the sciatic nerve on 5th March, 1945. Nerve found completely divided at the brim of the sacro-sciatic foramen. Suture not possible. Injection on 16th April, 1945. Short relief. Chain divided on 9th May, 1945. Complete relief. Discharged on 11th October, 1945.

10. *Case 29.*—Median causalgia. Shell wound, right forearm and right thigh. Severe burning pain of hand came on four days after injury. Paralysis of all ulnar muscles. Pain also in the sole of the right foot but not severe. Injection of dorsal chain on 21st March, 1945. Short relief. Chain divided on 26th March, 1945. Complete relief. Pain in sole of foot subsided by itself. In hospital.

11. *Case 28.*—Tibial causalgia. Gun-shot wound, left thigh, on 25th January, 1944. Moderately severe burning pain in sole of foot came on 14 days after injury. Can sleep at night. No loss of sensation. Paralysis of tibial and peroneal muscles. Exploration and suture of the peroneal nerve on 19th July, 1944. Tibial muscle had recovered spontaneously. Pain had completely subsided by 26th May, 1945.

12. *Case 32.*—Tibial causalgia. Shell wound, left thigh, on 3rd February, 1945. Moderately severe pain came on eight days after injury. Paralysis of peroneal muscles only. Loss of sensation in sole of the foot and

peroneal area. Posterior tibial artery denuded of its sympathetic fibres behind the medial malleolus on 20th May, 1945. Complete relief of pain. In hospital.

13. Case 11.—Median causalgia. Shell wound, right upper arm, on 7th June, 1944. Median causalgic pain noticed on 16th June, 1944. Brachial artery aneurysm noticed on 14th July, 1944. Aneurysm explored on 6th November, 1944. Arterial, saccular, median nerve found adherent to its wall. Carefully separated. Aneurysm excised. Pain subsided by itself gradually. Free of pain from 17th February, 1945.

14. Case 9.—Median causalgia. Gun-shot wound, left arm, on 21st May, 1944. No paralysis. No loss of sensation. Injection on 8th November, 1944. Complete relief of pain. Injection repeated on 8th January, 1945, because slight pain had recurred. Complete relief.

All the case summaries are not given to avoid repetition. The cases given above are sufficiently representative. Case 30 requires some comment. It shows that causalgic pain can occur with the nerve supplying the limb completely divided. That again would lead us to the conclusion that all the sympathetic fibres do not run with the main nerve of the limb. They either join it later or reach their destination *via* the blood vessels.

Another interesting point elicited during treatment of these cases was the result of experimental stimulation of the lumbar sympathetic trunk during operation. In three cases the lumbar sympathetic chain was exposed under local anæsthesia taking good care that the chain itself was not affected. On stimulation of the chain below the second lumbar ganglion with rapid faradic current little or no pain resulted, but compression or pinching of the nerve fibres produced marked pain which the patient vaguely referred to the leg on the same side. The pain could not be accurately localized, but all the patients maintained that it was felt deep down in the leg. In spite of carefully controlled laboratory experiments conducted on animals (Burgert and Livingston, 1931), the above experiments would go to show that in human beings at least pain fibres of some sort travel through the sympathetic chain.

Another noticeable fact about these cases of causalgia was the constancy of the site of the pain. Irrespective of the level of the lesion in the median nerve, the pain always started in the lateral half of the palm of the hand. The level of the lesion in the nerve varied from the axilla to the palm of the hand, but the pain always started in the same area of the hand. Similarly, the lesion in the tibial nerve varied from the buttock to the leg, and yet the pain was always felt in the sole of the foot. One wonders if there is not a close similarity between the causalgic pain and the visceral pain with which we are so familiar. The character of the pain in the two, no doubt, varies but that can be explained by the difference in stimuli in the two cases. The focus of irritation in causalgia lies in the intraneural fibrosis in which the central fibres of the divided nerves are involved. Impulses from this focus of

irritation set up changes in the spinal or thalamic centres. This would explain why causalgia was so commonly seen among Gurkhas and also why the cases of causalgia diminished to a negligible number after the general use of penicillin. This view of ætiology of causalgia is my own interpretation of facts always known. It is put merely as a suggestion.

Summary

1. Thirty-two cases of causalgia are described.
2. Their treatment by sympathectomy is discussed.
3. Case histories of some of the cases are included.

My thanks are due to Brigadier D. Denny-Brown, consulting neurologist, India, and Lieut.-Colonel R. A. Elliot, R.A.M.C., advisor in neurology, for valuable suggestions, and to General Gordon Willson, D.M.S., India, for permission to report the cases.

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PSYCHIATRY IN BURMA AFTER RE-OCCUPATION

By R. M. LLOYD-STILL
LIEUTENANT-COLONEL, I.M.S.

I ARRIVED in Burma on the 10th September, 1945, and was appointed in Cas (B) as Officer Commanding, Mental Hospital. This at that time only existed on paper. A few old demented and criminal insanes who had survived the Japanese occupation were accommodated in the local jail. The old Mental Hospital which was a comparatively new building, and before the war accommodated over 1,000 patients, presented a grim picture due to our bombing. This hospital had been one of the best in the east with spacious grounds, extensive gardens, big dairy and every facility for occupational therapy, etc. It had been used by the Japanese as a wireless transmitting station and the Indian national army were kindly permitted to have a hospital there! Many buildings had completely disappeared—the female section no longer existed and it was difficult to recognize the European wards or the hospital block.

The first problem was to find accommodation and a small jail which at one time was the Borstal Institute was decided upon and efforts were then made to get possession from the military authorities. Early in October the move was made and the place was tidied up. This

was rather like a jungle; petrol tins and shell cases were scattered all over the place. The wells contained, among other things, cartridges and Japanese hand grenades.

The patients soon adapted themselves to their surroundings. The wards had been partitioned off into wooden cages by the Japanese and there was a large bomb-proof shelter which after it had been demolished also provided us with timber. These were removed and converted into beds, benches and tables, etc., as furniture was very difficult to obtain.

Patients' clothing which before the war had been weaved on the premises by the patients themselves presented some difficulty which was largely solved by means of obtaining a number of parachutes from army salvage and converting them into clothes.

There were no records, no books, no forms, no penal code, no courts manual and no copy of the Lunacy Act to refer to. The hospitals in India responded to my requests and copies were sent which were printed by the government press which was now functioning. A few copies of the courts manual were obtained on loan from the judicial authorities.

Gradually the old staff returned from India and the few who had remained behind reported for duty. Two experienced doctors belonging to the pre-war mental hospital arrived from India and modern treatment was instituted forthwith. There was no nursing staff until early in December when a matron and two sisters were appointed. Later, one of the sisters resigned her job, leaving only the matron and one sister. Although the nursing staff was very inadequate and unfortunately remains so, our problem with regard to treating patients with insulin shock and nursing sick insanes was considerably eased.

TREATMENT

Convulsion therapy.—Since October 1945 to the end of April this year 366 injections of leptozole (made by Boots Pure Drug Co., Ltd.) have been given for the convulsion treatment of various types of insanity. I find this drug vastly superior to cardiazol as there is no apprehension and until an electrical convulsion therapy apparatus can be obtained there is no doubt as to its great value. In any case there is no electricity at present. Sixty-two cases were treated by means of leptozole injections. Out of these 29 cases were discharged cured, 26 discharged improved and 7 cases showed no change in their mental conditions.

Insulin-shock therapy.—Ten cases were treated with increasing doses of insulin. Seven of these cases were discharged recovered, two improved and one patient died of irreversible coma.

Dementia paralytica.—Fifteen cases of dementia paralytica have been admitted during the last six months.* Four of these cases were

treated with two courses of penicillin 2.4 m.u.—40,000 units every 3 hours, night and day for a week at a time. They all showed improvement physically and slight mental improvement. As no further penicillin was available further treatment of dementia paralytica cases by this method had to be suspended. Dementia paralytica cases are now being treated by means of induced pyrexia with inoculations of malarial blood followed by tryparsamide.

Pre-frontal leucotomy.—Three patients who showed no improvement after extensive convulsion therapy and insulin were operated on for pre-frontal leucotomy by the military neuro-surgeon who fortunately was stationed in the vicinity. The first patient, a Chinese youth, suffering from schizophrenia—catatonic type, who was impulsive, negativistic, resistive and dirty—became pleasant, clean and amenable and now works in the hospital. Second, a Burman, age 45, an ex-clerk, who had delusions of persecution with auditory hallucination and who was suspicious, dirty and seclusive, has improved remarkably after the operation. Though he still hears the voices, these no longer trouble him—he behaves normally, converses pleasantly and adapts himself well to the surroundings. The third case was a young Burmese woman, who was in a state of chronic excitement with schizophrenic features. Unfortunately she has not so far shown any improvement in her mental condition though it is now nearly a month after the operation. The first two patients showed improvement within the first week of the operation.

One hundred and seventy patients have been admitted since the re-opening of the hospital. Out of these 95 patients have been discharged recovered (56 per cent). This percentage of recoveries is far above the pre-war rate (26 per cent).

Nevertheless, in spite of our initial difficulties, a jail which is far from suitable for a modern mental hospital, being very limited in area and having too close proximity between male and female patients, will have to suffice for the present until the old hospital is repaired.

Everything possible is done to make convalescent patients contented and happy and what little ground is available is used partly for patients' games and the remaining space as vegetable gardens which have already given a good yield this season.

Summary

1. The difficulties encountered in recommending the care and treatment of mental patients in Burma and our efforts to establish psychiatry on modern lines, first under the military administration and later under the civil government, are described.

2. Intensive treatment with modern psychiatric methods are discussed and the very favourable discharge rate is compared with the pre-war percentage.

* In a later communication the author agrees that 'compared with India the incidence of G.P.I. in Burma is very high.'—EDITOR, I.M.G.

3. Three cases of pre-frontal leucotomy are described briefly.

I wish to thank Drs. Chari and Naidu and the nursing staff (consisting of matron and one sister) for their able assistance and their willing co-operation, and Colonel M. L. Treston, C.B.E., I.M.S., Inspector-General of Civil Hospitals, Burma, Rangoon, for his permission to publish this short note.

A NOTE ON THE USE OF SULPHONAMIDES IN THE TREATMENT OF PLAGUE IN THE FIELD

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and

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THE value of sulphonamides in the treatment of bubonic plague is now well established. Sokhey and Dikshit (1940) showed sulphathiazole to be possessed of remarkable therapeutic action in experimentally induced plague infection in mice. On the basis of this experimental work, extensive field trials were carried out with a grant from the Indian Research Fund Association. The first field trial was conducted at Bettiah, Bihar, from January 1940 to April 1940. Bettiah Raj erected a temporary hospital and provided other facilities for a controlled trial to be conducted by workers from the Haffkine Institute. Two hundred and seventy-five cases of plague were treated and the therapeutic action of sulphapyridine, sulphathiazole and Haffkine Institute anti-plague serum was studied. Later, H. E. H. the Nizam's Government invited the Haffkine Institute to conduct field trials at Latur. The State built a temporary plague hospital and provided all the necessary facilities. This trial lasted from November 1940 to April 1941. During this trial, 267 cases were treated. A third trial was also carried out at Latur from December 1941 to March 1942 and 140 cases were treated. The same drugs were tried during these field trials. Later at Poona, from November 1943 to February 1944, the comparative value of sulphathiazole and sulphadiazine was tested.

Fuller details of these trials have been described by Wagle *et al.* (1941), Sokhey and Wagle (1943) and Wagle (1944). Salient features of the trials are, however, given here for ready reference.

Methods

Diagnosis.—On admission every patient was examined for a bubo and other clinical signs of plague. Next, before any treatment was given, 0.5 c.cm. of blood was drawn from a vein of each patient and plated in equal quantities on two agar slopes. This was done to determine the presence or absence of plague septicæmia at the time of admission and its severity. These slopes were incubated at room temperature

for two days and if the cultures remained sterile bubo was punctured with a syringe and the fluid drawn up plated on agar slopes to confirm diagnosis. If 0.25 c.cm. of blood gave less than 10 colonies, it was noted as a case of mild septicæmia while cases with more than 10 colonies in 0.25 c.cm. of blood were considered as cases of severe septicæmia. Many severe septicæmic cases showed over 1,000 colonies for 0.25 c.cm. of blood and some gave even a confluent growth.

During the field trials it was noticed that the most important single factor which decided the issue in human bubonic plague was the development and degree of septicæmia. If the lymph-gland prevented the spread of infection to the blood stream and the infection remained localized, spontaneous recovery usually resulted. On the other hand if the organisms passed the lymph-gland and septicæmia resulted, death almost invariably followed, unless an effective curative agent was given to control the infection. Among the control cases, several, which had no septicæmia at the time of admission, developed septicæmia later and died. While with the three therapeutic agents under test septicæmia seldom developed if it was not present at the time of the exhibition of the agent. Thus a truer picture of the results of a given treatment is obtained if only those cases are considered which had septicæmia at the time the treatment was started. For this reason results of trials are given in two tables. One table shows the results of the treatment in 'all cases' and the other of 'cases with plague septicæmia at the commencement of treatment'.

Division of cases.—When two or more different treatments were given, they were given in strict rotation, no selection of cases was made. Yet the composite figures of all the trials given in the table do not total up to an equal number for each drug. The principal reason is that in our earlier trials, we had used only anti-plague serum, and in the first trial of the present series, we tested serum, sulphapyridine and sulphathiazole, in the next one only sulphapyridine and sulphathiazole were tested, and in the third one sulphathiazole and sulphathiazole plus serum, while only in the last (fourth) trial at Poona did we try sulphadiazine, and compared its action against that of sulphathiazole.

Dosage.—The sulphonamides were given in a large dose on the first day with a view to getting the desired concentration in the blood quickly. The concentration was maintained by smaller doses on subsequent days. The drugs were not usually administered for more than 7 to 10 days.

During the trial at Bettiah in 1940, we gave sulphapyridine in a dosage of 3.5 gm. on the first day and 3.0 gm. each succeeding day for 7 days. In this trial we were not equipped to measure the concentration of the drug in blood and so we were not sure whether we had used an adequate dosage. During the next trial at Latur in 1940, we tried a dose of 9.5 gm. the

first day and 8 gm. per day for the next four days and a smaller dose later when necessary. This dosage produced very serious toxic symptoms and we reduced the dosage to 8 gm. the first day and 3 to 4 gm. per day during the next 4 days. The smaller dosage gave a concentration in blood of 5 to 10 mg. per cent.

Similarly in the case of sulphathiazole we tried different dosage. In the 1940 Bettiah trial, when we did not measure the concentration in blood we gave it in a dosage of 3.5 gm. the first day and 3.0 gm. a day each succeeding day for 7 days. Then in 1940 Latur trial, we tried a dosage of 14 gm. the first day and 9 gm. each succeeding day for 7 days in 56 cases but found it rather toxic. This dosage gave a concentration of 10 to 20 mg. per cent and showed no better results than the smaller dosage given later, which was 10 gm. the first day and 7.5 gm. a day on subsequent days. This smaller dosage gave a concentration of 5 to 10 mg. per cent and the results obtained with it were as good as with the higher dosage. In 1943 Poona trial, sulphathiazole was given in a dosage of 10 gm. the first day and 6 gm. a day on subsequent days. This gave a concentration of 5 to 8 mg. per cent and the results were as good as the higher dosage of 14.0 gm. the first day and 9 gm. on subsequent days that was used again in a few serious cases in this trial.

In the case of sulphadiazine which was tried in the 1943 Poona trial, two different dosages were given. The higher dosage of 14 gm. the first day and 6 to 9 gm. on subsequent days was tried in a few very serious cases and gave a concentration of 15 to 20 mg. per cent, but as the results were the same as with the smaller dosage, it was discontinued. The smaller dosage used was 10 gm. on the first day and 6 gm. a day on subsequent days. This gave a concentration of 10 to 15 mg. per cent and also as good results as with the higher dosage. We have not been able to try a still smaller dosage, but good results have been obtained with the dosages given above.

Controls.—During the field trial at Bettiah, the first trial of the present series, like the field trials reported in the earlier trials, alternate admissions were treated with iodine intravenously. This treatment was in vogue in the hospitals at that time. The cases so treated were considered as controls. But during the succeeding three trials we did not keep any controls, because during the first trial of this series and the previous field trials, we had had 149 controls and these had provided all the necessary information.

Results.—The results of all the field trials are given below in two tables. Table I gives figures for all cases of plague with or without septicæmia at the commencement of the treatment, while table II gives figures for cases with septicæmia at the commencement of the treatment. As we have noted before, the presence of septicæmia at the commencement of the treatment is the

most important factor which determines the issue. Thus a consideration of cases with septicæmia at the commencement of the treatment gives a better idea of the relative merits of the different treatments.

TABLE I*

Summary of the results of all the field trials and of all cases treated with or without septicæmia at the commencement of the treatment.

Treatment	Number of cases	Number of deaths	Case mortality, per cent
Anti-plague serum ..	157	37	23.5
Sulphapyridine ..	122	33	27.0
Sulphathiazole ..	305	64	21.0
Sulphathiazole cum anti-plague serum.	60	12	20.0
Sulphadiazine ..	81	10	20.9
Controls: iodine intravenously.	149	80	53.6

TABLE II*

Cases with plague septicæmia at the commencement—summary of the results of all the field trials

Treatment	Number of cases	Number of deaths	Case mortality, per cent
Anti-plague serum ..	71	36	50.7
Sulphapyridine ..	62	31	50.0
Sulphathiazole ..	1,328	55	41.6
Sulphathiazole cum anti-plague serum.	25	8	32.0
Sulphadiazine ..	43	9	20.9
Controls: iodine intravenously.	75	68	91.0

* Cases which died within 24 hours of admission have not been included in these tables nor have they been mentioned in this paper. Fuller details will be given when all data are published.

Comments

If we take table I which gives the results of all the cases treated—with or without septicæmia at the commencement of the treatment—we find a case mortality of 53.6 per cent among the controls, i.e. cases treated with iodine given intravenously. This treatment was the routine treatment in hospitals when we began our work. There is reason to believe that even iodine did save some cases, specially in the early stages of the disease in which septicæmia had not yet developed. This case mortality of 53.6 per cent is reduced by the treatments we are discussing from 12.3 per cent to 27.0 per cent. This reduction in case mortality is significant.

Now if we take table II which gives the cases which had septicæmia at the commencement of the treatment, we have a case mortality of 90.7 per cent among the controls, i.e. cases treated

with iodine given intravenously. Anti-plague serum reduced the percentage case mortality to 50.7, sulphapyridine to 50.0, sulphathiazole to 41.6 and sulphadiazine to 20.9. Reduction in mortality between the controls and the treated cases is highly significant, but it is not certain whether the apparent differences between the different treatments are equally significant. Sulphadiazine appears to give the best results, but the total number of cases treated with this drug is small and for this reason the apparent difference is not significant.

Sulphadiazine, however, did show a certain advantage over both sulphathiazole and sulphapyridine: it induced little or no nausea and vomiting and did not give rise to dermatitis even in a single case. Sulphapyridine was definitely more toxic than either sulphathiazole or sulphadiazine and it was found easier to maintain blood concentration of the drugs with sulphapyridine and sulphadiazine. Toxæmia due to the disease was most easily brought under control with anti-plague serum and the results seemed to be best when serum was used with sulphathiazole. But sufficiently large number of cases were not treated with serum plus sulphathiazole to decide the issue.

Suggestions for future field trials

We have so far tried only sulphapyridine, sulphathiazole and sulphadiazine. Newer sulphonamides are already available and will require to be tried if they prove to be effective in experimental infection in mice. It is necessary that such trials should be conducted on some common plan, so that statistically comparable results are obtained at different stations. In addition the suggestion we are offering will prove helpful in the routine use of any of the selected drugs in the treatment of plague cases.

1. Hospitalization

To carry out the suggested plan, it is necessary to hospitalize cases. For this purpose, it is usually necessary to put up temporary hospitals. Such hospitals must have adequate facilities both as regards personnel and material comfort and care of the patient, and the necessary laboratory facilities. On the basis of a 30 bedded hospital, it was found that the following personnel was needed: 1 medical officer in charge; 2 assistant medical officers; 2 laboratory assistants; 4 nurses; 3 male ward attendants; 3 ayahs; 2 male sweepers and 2 female sweepers and the necessary personnel for cooking and serving food to the patients and the staff.

2. Classification of cases

As we have said before, the most important single factor which decides the issue in human bubonic plague is the development and degree of septicæmia. Untreated almost all cases which develop septicæmia die. Therefore, for evaluating the curative action of a drug in the

treatment of plague, it is necessary to determine the presence or absence of septicæmia when the treatment is commenced. It is also necessary to keep a watch over the sulphonamide having any adverse effect on the hæmatopoietic system of the patient. To do this, before the treatment is commenced, 5 c.cm. of the patient's blood are drawn and 0.5 c.cm. of this blood is distributed on two agar slopes in equal quantities, i.e. 0.25 c.cm. on each slope. The rest of the blood, i.e. 4.5 c.cm., is delivered into a 25 c.cm. conical flask containing 9 mg. of potassium oxalate. This blood is then used for making hæmoglobin estimation, red cell and white cell count and a differential count. The agar slopes on which the patient's blood has been spread are incubated for two to three days at room temperature. At the end of this time, the plague colonies which grow on these slopes are counted. If the number of colonies is less than 10 in 0.25 c.cm. of blood, the case is classified as of mild septicæmia and if the number of colonies is over 10, the case is classified as of severe septicæmia. If no colonies grow, the case is marked as non-septicæmic.

Certain patients have idiosyncrasy to the drug. When administering sulphonamides, it is necessary to make sure that the drug does not produce toxic symptoms on the hæmatopoietic system as evidenced by acute hæmolytic anæmia or agranulocytosis or severe leucopenia. So it is necessary to make blood counts before the drug is given and thereafter every 48 hours till the drug is stopped.

3. Dosage

Sulphathiazole.—An initial dose of 2 gm. is given followed by 2 gm. four hours later. Thereafter 1.5 gm. are given every 4 hours till the end of the first 24 hours. One gramme is then continued four-hourly on subsequent days. The drug is stopped 2 days after the temperature comes to normal and the patient's general condition improves. In any case, the drug should not be given for more than 10 days.

Sulphadiazine.—An initial dose of 4 gm. should be given followed by 2 gm. 4 hours later. One gramme is continued every 4 hours subsequently till the temperature and pulse have remained normal for two days. It is, however, not desirable to give the drug for more than 10 days at a time.

Both the drugs, as far as possible, should be given orally, but in cases which are comatose or unable to swallow for any reason, parenteral administration may be resorted to. In very severe cases, it is advisable to give the initial dose of 2 gm. intravenously and the following doses orally. This will raise the concentration of the drugs in the blood quickly and their action will begin immediately. The dosage of the two drugs given above gives a blood level of 5 to 10 milligrammes per 100 millilitres of free sulphathiazole and 10 to 15 milligrammes per 100 millilitres of sulphadiazine. To maintain

this concentration, however, it is necessary to give the drugs every 4 hours regularly night and day.

4. Laboratory facilities

Every effort should be made to create laboratory facilities to make measurements of concentration of sulphonamides in blood. For this purpose, Bratton and Marshall's method (1939) is usually employed. It is quite easy to carry out. Briefly, the method is as follows :—

Two c.cm. of oxalated blood are diluted with 30 c.cm. of 0.17 saponin solution. After 2

suppression of urine, agranulocytosis and drug fever develop, the drugs must be stopped immediately and fluids forced orally and through the vein, to eliminate the drugs from the system. If mild toxic symptoms such as vomiting, spasmodical abdominal pain and pain in joints and muscles appear, it is not necessary to stop the drug, but the dosage should be reduced to half and continued.

6. Case sheets and records

The case sheets should be carefully maintained and the information abstracted on some such form as appended :—

Date of admission	Case No.	Treated or control	Age	Sex	Duration	Date of inoculation	Site of bubo	Bubo culture	Blood culture	TREATMENT WITH	Repeated blood culture	Result	REMARKS

minutes (after hæmolysis) 8 c.cm. of a 15 per cent solution of trichloroacetic acid are added to precipitate the proteins. After 2 to 3 minutes the precipitated proteins are filtered off and 10 c.cm. of the clear filtrate are taken for the estimation of free sulphonamide. To 10 c.cm. of this solution, 1 c.cm. of 0.1 per cent aqueous sodium nitrate solution is added and shaken well. After 2 minutes, 1 c.cm. of 0.5 per cent solution of ammonium sulfonate is added and shaken well. After 2 minutes, 1 c.cm. of a 0.1 per cent solution of the coupling component β -aminoethyl naphthylamine hydrochloride is added and shaken well. The blue-violet colour that develops is compared with a standard solution of the sulphonamide solution of concentration 0.25 or 0.5 mg. per cent, similarly treated. The concentration obtained multiplied by 20 (the degree of dilution of the blood sample made) gives the concentration of the drug in the blood expressed as mg. per cent.

Determination of acetylated sulphonamide.—10 c.cm. of the protein-free colourless filtrate are treated with 1 c.cm. of 4 N HCl and heated on the steam bath for 30 minutes. The solution is made up to 10 c.cm. and the estimation is carried out as described for the determination of the concentration of the free drug.

5. Toxic symptoms

Majority of the patients bear the drugs well, but in few cases who are peculiarly susceptible to the drugs, toxic symptoms develop in spite of the correct dosage. These symptoms, to a very large extent, can be reduced if an alkaline mixture containing citrates is given every four hours after each dose of the drug and the patients encouraged to drink plenty of water so as to maintain a urinary output of 1,000 to 1,200 c.cm. a day. If severe toxic symptoms such as jaundice, acute hæmolytic anæmia,

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A SIMPLE METHOD OF BLOOD PROTEIN ESTIMATION

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ESTIMATIONS of blood proteins and albumin-globulin ratios are coming to occupy a place of increasing importance in medicine. These estimations are usually carried out only in institutions with biochemical laboratories, and the methods usually used, such as the Kjeldahl method, necessitate special apparatus and equipment. Many hospitals do not have these facilities. There is, therefore, a great need for a simpler method which can be more widely applied.

The method here to be described is one which has been used for the last year in the Calcutta School of Tropical Medicine in very large numbers of cases of all kinds with satisfactory results. Many enquiries for details of this method have reached us and therefore we are preparing this note describing the method. In a later publication we propose to

give in detail the findings of this method applied in patients of various kinds and in different diseases and in different forms of malnutrition.

Estimation of total proteins

The principle of the method is that if the specific gravity of plasma is known, the blood proteins can be estimated from the formula. $P = 343 (\text{Gp.} - 1.0070)$ where P = total plasma proteins and Gp. = specific gravity of plasma.

The specific gravity of plasma is measured by the method of Phillips *et al.* (1945) by dropping drops of plasma into solutions of copper sulphate of different specific gravities.

The preparation of these copper sulphate specific gravity bottles is a matter requiring considerable care, but it can be done almost anywhere. The steps are as follows:—

The preparation of the standard solution of copper sulphate of specific gravity 1.100.—Copper sulphate, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as pure as possible is obtained in the form of fine crystals. It should be of at least B.P. standard, and better still of analytical standard. 170 gm. of these fine pure copper sulphate crystals are accurately weighed. The amount of water to be added to this weighed amount of copper sulphate to prepare the stock solution of specific gravity 1.100 varies with the temperature of the water at the moment of addition and is shown in table I (*see appendices*) quoted from Phillips *et al.* (1945). The required amount of water is carefully measured with a one-litre measuring flask, the extra few c.cm. over the litre being accurately measured with a 10 c.cm. graduated pipette. In making up the standard solution with the weighed amount of copper sulphate and the measured amount of water, care must be taken that not one grain of copper sulphate or one drop of water is left unused.

In the United States enterprising firms are putting on the market: (1) sealed bottles containing exactly 170 gm. of pure copper sulphate fine crystals ready to be used for making up stock solutions by the method described in the text, and (2) sealed bottles containing solutions of specific gravity 1.100 at 25°C. ready for dilution to make the standard solutions needed.

Phillips *et al.* (1945) give another method of preparing stock solutions of specific gravity 1.100 without even the use of a balance. This method involves two steps: (a) the preparation of a saturated solution of copper sulphate by shaking up fine crystals, 1 lb. in 625 c.cm. of distilled water at room temperature, the mixture being shaken vigorously for five minutes and the temperature of the mixture being taken immediately at the end of this five-minute period, the solution being then decanted from the bottle and filtered as quickly as possible. This filtration is best done in two stages, first through a wad of cotton-wool which removes all except a few very fine crystals and then through a coarse filter paper, which removes the rest, (b) the saturated solution immediately

after filtration is diluted with water according to the instructions given in table II (*see appendices*), the amount of solution taken for dilution to 1,000 c.cm. depending upon the temperature of the saturated solution at the moment saturation was ended, i.e. immediately after the five minutes' shaking. The stated amount of saturated solution is measured in a 500 c.cm. cylinder and then transferred to a one-litre volumetric flask, the cylinder being allowed to drain for two minutes. The one-litre flask is then filled up to the mark with distilled water and inverted ten times for mixing. The mixing results in shrinkage. The flask is allowed to stand for a minute to allow the solution to drain down the neck, and then enough water is added to bring the meniscus back to the mark. The flask is then stoppered and the solution mixed, and the solution is then stored in bulk. This is the stock solution of S.G. 1.100 at 25.0 centigrade.

In our hands, this method though fairly satisfactory, has not been as satisfactory as the method described above.

Preparation of sets of standard solutions from stock solution

The principle is as follows: To produce a solution of, for example, 1.030 specific gravity, 29 c.cm. (one less than the last two digits of the required specific gravity) of the stock solution of S.G. 1.100 is placed in a 100 c.cm. volumetric flask and the flask is filled to the 100 c.cm. mark with distilled water. The solution is mixed, transferred to a suitable bottle and securely stoppered to prevent evaporation, similarly with any other desired specific gravity. For more accurate work a table is quoted from Phillips *et al.* (1945) (*see appendices*).

For studying blood proteins, specific gravity bottles ranging from 1.014 to 1.046 are prepared, although the higher ranges are only needed when there is much hæmoconcentration for example in cholera, and the lower ranges are needed only when there is marked hypoproteinæmia. The range from 1.014 to 1.046 is best covered in steps of 0.002 and a set of 17 bottles is needed. A set of 9 bottles in steps of 0.004 will give results quite accurate enough for ordinary clinical work.

The test for blood protein estimations, 3 c.cm. of blood is taken with a syringe from the vein and put in a tube containing 3 mg. of ammonium-potassium oxalate mixture. These tubes are prepared in advance by pipetting into each tube 0.15 c.cm. of a 2 per cent solution of Heller and Paul's oxalate mixture. (This consists of 3 gm. ammonium oxalate and 2 gm. of potassium oxalate dissolved in 200 c.cm. of water. These tubes are then dried in a hot air oven; the solution evaporates and leaves the dry ammonium-potassium oxalate mixture. The tubes can be prepared in large numbers and kept ready for use.) Immediately the blood is placed in the tube, it is shaken fairly thoroughly to

prevent coagulation but not enough to produce hæmolysis. It is then centrifugalized to separate off the plasma.

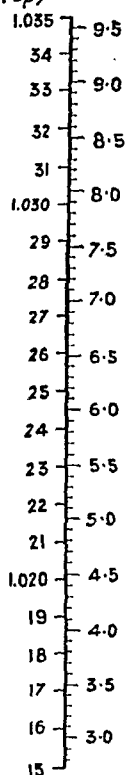
About $\frac{1}{2}$ c.cm. of plasma is taken into a fine glass pipette with a rubber teat, and drops of plasma are allowed to fall from the pipette into the CuSO_4 solutions of different specific gravity from a height of about 1 cm. The drop breaks through the surface film of the solution and penetrates 2 or 3 cm. below the surface. Within 5 seconds, the momentum of the fall is lost, and the drop begins to rise, becomes stationary, or continues to fall. The gravity of the drop relative to the solution does not change appreciably until the drop has been immersed into the solution for another 10 or 15 seconds. It is its behaviour during this interval which is important. Drops are dropped into bottles of different specific gravities until that bottle is found which produces the stationary drop during this interval. After 20 seconds or so all drops change specific gravity and fall to the bottom. In practice it is often found that a drop rises slightly in one bottle, say 1.032, and falls slightly in the next bottle (say 1.030) in which case the S.G. is recorded as 1.031. If the bottles are at steps of 0.004, similar adjustments will more often be needed and, to quote an example, a slight fall in 1.030 and a more marked rise in 1.034 will justify a reading of 1.031 and not 1.032. A four-ounce bottle of the copper sulphate solutions of any specific gravity can be used until about one hundred (small) drops have been dropped in it. It should then be replaced.

The specific gravity of the plasma being thus determined, the plasma proteins in gm. per cent can be estimated from the formula $P \approx 343^* (\text{Gp.} - 1.0070)$, or more simply the plasma proteins can be read off from the line chart given here.

The limitations of total protein estimations

This matter cannot be discussed here in detail. It

Plasma
Specific proteins
gravity (gm/100 cc)
(Gp)



* This factor 343 is the one originally derived by Moore and Van Slyke (1930) and used in the original publication on the copper sulphate method of blood protein estimation by Phillips *et al.* (1943). In the booklet by Phillips *et al.*, 1945, from which much of the information here given is quoted, the factor 360 is recommended, but we have found that the results given by this factor are consistently high and prefer to use the figure 343. Even with factor 343 the results are sometimes rather higher than one expects.

can only be stated that in many pathological conditions the total protein will be within normal limits, but the albumin-globulin ratio may be completely reversed or even more than reversed. It is, therefore, highly desirable that in addition to estimating total proteins the albumin-globulin ratio should also be determined.

Albumin and globulin fractions

The principle of the method here described is as follows: The total protein having been estimated by the copper sulphate specific gravity method, the albumin (and globulin by difference) is estimated by the biuret reaction, after separation of the globulin by precipitation with half saturated ammonium sulphate the estimation being done in a colorimeter of Klett or other similar type, the plasma itself (of total protein content already determined) being used as the standard.

The procedure is as follows: The total protein content of the plasma is estimated by the method described above.

One c.cm. of plasma is diluted to 10 c.cm. with isotonic sodium chloride solution. Five c.cm. of this diluted plasma are mixed with 5 c.cm. of saturated $(\text{NH}_4)_2\text{SO}_4$ solution. After 20 minutes the globulin precipitate is filtered off through a fine filter paper (5.5 cm.) in a small funnel. If the filtrate is not clear, it should be passed through the paper a second time. The filtrate contains the albumin.

Four c.cm. of this albumin filtrate (containing the albumin from 0.2 c.cm. of plasma) is diluted with 4 c.cm. of water, and to this is added 0.2 c.cm. of 10 per cent sodium tungstate solution, and 0.2 c.cm. of $\frac{2}{3} N \text{H}_2\text{SO}_4$, mixing thoroughly after each addition. The albumin is precipitated.

For a standard, 1 c.cm. of the original diluted plasma (0.1 c.cm. of plasma) is diluted with 2 c.cm. of water and to this is added 0.2 c.cm. of 10 per cent sodium tungstate and 0.2 c.cm. of $\frac{2}{3} N \text{H}_2\text{SO}_4$, mixing after each addition. All the proteins are precipitated.

Both the tubes, the albumin tube and the standard, are centrifuged, the supernatant fluid poured off and the tubes inverted and stood on filter paper to drain. The precipitates are dissolved in 3.4 c.cm. of $N \text{NaOH}$, 0.1 c.cm. of 20 per cent CuSO_4 solution is added, followed by 1.5 c.cm. of water. The tubes are stoppered and shaken for two minutes. Any excess of $\text{Cu}(\text{OH})_2$ is centrifuged down, and the violet-coloured solutions are decanted and compared in a colorimeter.

The calculation is based on the formula: albumin (in grammes per cent) $= \frac{S}{A} \times \frac{1}{2} \times P$, where S = the colorimetric reading of the standard tube, A = the colorimetric reading of the albumin tube, and P = the total protein content of the plasma as estimated in grammes

per cent by the copper sulphate specific gravity method.

Note.—The factor $\frac{1}{2}$ is necessitated by the fact that the standard tube contains the protein from only 0.1 c.cm. of plasma while the albumin tube contains the albumin from 0.2 c.cm. of plasma.

Reagents needed—

- Isotonic saline.
- Saturated NH_4SO_4 solution.
- 10% sodium tungstate.
- $\frac{2}{3} N \text{H}_2\text{SO}_4$.
- $N \text{NaOH}$.
- 20% CuSO_4 .

Apparatus—

Suitable colorimeter, test-tubes, funnels, graduated pipettes, etc., are needed.

A few notes regarding colorimeters and their use may be desirable. The most accurate colorimeter is the photo-electric colorimeter, the standard and the albumin tubes being read separately. In this case the formula for calculating the albumin is different, the formula being $\frac{A}{S} \times \frac{1}{2} \times P$. Photo-electric colorimeters are however few and at present difficult to obtain, so we will here discuss mainly other colorimeters. The two tubes, standard and albumin, can be compared, one against the other, in a colorimeter of the Klett type. Sometimes the colour tints of the different solutions are not quite identical, and there may be a little difficulty in matching the two halves of the field.

With certain colorimeters, better results are obtained by the use of the colorimeter as a photometer, and comparing each tube, the albumin and the standard, separately against a standard gray screen, a suitable green filter being placed over the eyepiece.

The procedure is as follows: First the light on both sides of the colorimeter is made equal. Electric light is usually preferable to daylight since a fairly high intensity light is needed. A small piece of suitable light gray tinted glass as a screen is placed on the platform of the right-hand cup of the instrument, and this is screwed up until it touches the plunger. A suitable green filter is placed on top of the eyepiece of the instrument. The first fluid to be tested is poured into the left-hand cup and the height of the cup is adjusted until the two sides of the field seen through the green filter show exactly the same light intensity. The reading on the scale corresponding to the left-hand cup is then made. The procedure is repeated with the second tube, the standard, and the calculation is then made as described above.

We have used this method with the Klett colorimeter, but with our instrument the end points have not been very satisfactory, and better results have been obtained by direct comparison. With another instrument, however, in our possession, its use as a photometer by the method above described has given most excellent

results, the end points being very clear and the results extremely constant. This colorimeter has plungers consisting of hexagonal glass rods; the ordinary Klett has plungers with opaque sides and glass bottoms.

Albumin-globulin ratios

From the values obtained by the above methods of blood protein estimation the albumin-globulin ratios can be calculated. These ratios are of great importance in many conditions including many tropical diseases and other chronic conditions. In kala-azar, for example, the normal albumin-globulin ratio of between 1.7 and 2 to 1 is reversed or much more than reversed, and albumin-globulin ratio of 0.3 to 1 even lower may be encountered even when the total protein is within normal range or higher than normal. These abnormal values are due to diminished albumin and a greatly increased globulin fraction. A simple way of expressing the result of blood protein estimation consists of giving two values, first, the figure for the total blood protein and, second, the albumin-globulin ratio. In some conditions, however, for example hypoproteinæmia, a more important figure, is that of the albumin fraction in grammes per cent.

Some typical examples

The following examples, taken from our records of recent works, are quoted to indicate the types of finding which may be made in blood protein estimations by the methods described in this paper.

1. A normal healthy adult :—

(a) Total protein—

S.G. of plasma = 1.029.

Plasma proteins (from line chart)

= 7.5 grammes per cent.

(b) Protein fractions—

Colorimeter readings—

Albumin tube 9.0

Standard tube 11.1

∴ Albumin in grammes per cent

$$= \frac{S}{A} \times \frac{1}{2} \times 7.5$$

$$= \frac{11.1}{9} \times \frac{1}{2} \times 7.5$$

= 4.6 grammes (approx.).

Globulin = total protein minus albumin

= 7.5 - 4.6 = 2.9 grammes.

(c) Albumin-globulin ratio = 4.6 to 2.9

= 1.6 to 1 (approx.).

2. A case of nutritional œdema :—

(a) Total proteins—

S.G. of plasma = 1.020.

Plasma protein (from line chart)

= 4.4 grammes per cent.

(b) *Protein fractions—*

Colorimeter readings—

Albumin tube 23.0

Standard tube 18.9

$$\therefore \text{Albumin} = \frac{S}{A} \times \frac{1}{2} \times 4.4$$

$$= \frac{18.9}{23} \times \frac{1}{2} \times 4.4$$

$$= 1.8 \text{ grammes per cent (approx.)}$$

Globulin = total protein minus albumin

$$= 4.4 - 1.8$$

$$= 2.6 \text{ grammes per cent.}$$

(c) *Albumin-globulin ratio*

$$= 1.8 \text{ to } 2.6$$

$$= 0.7 \text{ to } 1 \text{ (approx.)}$$

3. A case of kala-azar:—

(a) *Total proteins—*

S.G. of plasma = 1.027.

Plasma protein (from line chart)

$$= 6.8 \text{ grammes per cent.}$$

(b) *Protein fractions—*

Colorimeter readings—

Albumin tube 21.6

Standard tube 12.6

$$\therefore \text{Albumin} = \frac{S}{A} \times \frac{1}{2} \times 6.8$$

$$= \frac{12.6}{21.6} \times \frac{1}{2} \times 6.8$$

$$= 2.0 \text{ grammes per cent (approx.)}$$

Globulin = total protein minus albumin

$$= 6.8 - 2.0$$

$$= 4.8 \text{ grammes per cent.}$$

(c) *Albumin-globulin ratio*

$$= 2.0 \text{ to } 4.8$$

$$= 0.4 \text{ to } 1 \text{ (approx.)}$$

4. A case of cholera (hæmoconcentration):—

(a) *Total proteins—*

S.G. of plasma = 1.040.

Blood protein (from line chart)

$$= 11.3 \text{ grammes per cent.}$$

(b) *Protein fraction—*

Colorimeter readings—

Albumin tube 7.3

Standard tube 8.2

$$\therefore \text{Albumin} = \frac{S}{A} \times \frac{1}{2} \times 11.3$$

$$= \frac{8.2}{7.3} \times \frac{1}{2} \times 11.3$$

$$= 6.3 \text{ grammes per cent (approx.)}$$

Globulin = total protein minus albumin

$$= 11.3 - 6.3$$

$$= 5.0 \text{ grammes per cent.}$$

(c) *Albumin-globulin ratio*

$$= 6.3 \text{ to } 5.0$$

$$= 1.26 \text{ to } 1 \text{ (approx.)}$$

General recommendations

The methods of blood protein estimation here described give results which, although less accurate than the modern version of the Kjeldahl method, are of the greatest value in clinical work in India, where malnutrition and diseases upsetting protein metabolism are so common. Moreover, these methods are applicable without any special laboratory apparatus and equipment, with exception that a colorimeter is needed.

Blood protein estimations are sometimes of value in diagnosis, for example, the diagnosis of nutritional diarrhoea, oedema and anaemia from dysentery and oedema or anaemia due to other causes. They are of considerable value in the management, treatment and prognosis of patients. For example, they give clear indications regarding the dietetic needs of patients; unless the blood protein values can be made to return to something like normal, the prognosis is not good; the discharge of patients from hospital with seriously abnormal blood protein values is inadvisable.

When the method is first put into practice by staff with no previous experience of the method, it is best to carry out the first few estimations on healthy normal adults to see if the results obtained are within normal range. If not, the accuracy of the specific gravity of bottles and the purity of the reagents should be checked. Usually, however, any intelligent doctor or technician has little difficulty in initiating the work. Once the method is working satisfactorily, intelligent assistants can be trained to do it. Thus one man can do several dozens of total blood protein estimations in one day, and in addition can carry out twelve or more estimations of fractions.

Summary

1. The method of total blood protein estimation by means of copper sulphate specific gravity bottles is described.

2. The total proteins having been estimated by the above method the albumin, and the globulin by difference, is estimated by means of the biuret reaction after separation of the globulin with half-saturated ammonium sulphate, the plasma itself of known total protein content being used as standard for comparison. The method of doing this is described.

3. These methods of blood protein estimation are strongly recommended for use in this country particularly in centres where biochemical laboratories are not available. Some sample findings in different conditions by these methods are given.

Acknowledgment

In the preparation of this paper free use has been made of the publication 'Copper sulphate method for measuring specific gravities of whole blood and plasma' by Phillips *et al.* For advice and help regarding the use of the biuret reaction for estimating protein fractions the authors are deeply indebted to Professor King of the Postgraduate Medical School, London, who suggested the method and provided the details.

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APPENDICES

TABLE I

Volumes of water to add to 170.0 of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ to prepare stock solution of S.G. 1.1000*

Temperature of water,		C.cm. of water to 170 gm. of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$
°C.	°F.	
10	50.0	1,003.6
12	53.6	1,003.8
14	57.2	1,004.0
16	60.8	1,004.3
18	64.4	1,004.7
20	68.0	1,005.1
22	71.6	1,005.5
24	75.2	1,006.0
26	78.8	1,006.5
28	82.4	1,007.0
30	86.0	1,007.7
32	89.6	1,008.3
34	93.2	1,008.9
36	96.8	1,009.6
38	100.4	1,010.4
40	104.0	1,011.2

*The solution contains 1,002.4 gm. of water per 170 gm. $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The volumes of water given in the table are 0.8 c.cm. per litre more than theoretical in order to allow for adherence of this amount to the inside of the flask after 2-minute drainage.

TABLE II

Volume of saturated copper sulphate solution to dilute to 1 litre to prepare stock solution of S.G. 1.1000

Temperature of the saturated solution at the time of saturation,		Volume of solution to dilute to 1 litre,	Temperature of the saturated solution at the time of saturation,		Volume of solution to dilute to 1 litre,	Temperature of the saturated solution at the time of saturation,		Volume of solution to dilute to 1 litre,
°C.	°F.		°C.	°F.		°C.	°F.	
10.0	50.0	587	20.0	68.0	489	30.0	86.0	424
10.5	50.9	581	20.5	68.9	485	30.5	86.9	421
11.0	51.8	575	21.0	69.8	481	31.0	87.8	418
11.5	52.7	569	21.5	70.7	477	31.5	88.7	415
12.0	53.6	563	22.0	71.6	474	32.0	89.6	412
12.5	54.5	557	22.5	72.5	470	32.5	90.5	410
13.0	55.4	552	23.0	73.4	466	33.0	91.4	407
13.5	56.3	546	23.5	74.3	463	33.5	92.3	404
14.0	57.2	541	24.0	75.2	459	34.0	93.2	401
14.5	58.1	536	24.5	76.1	456	34.5	94.1	398
15.0	59.0	531	25.0	77.0	453	35.0	95.0	395
15.5	59.9	527	25.5	77.9	450	35.5	95.9	392
16.0	60.8	522	26.0	78.8	446	36.0	96.8	389
16.5	61.7	518	26.5	79.7	443	36.5	97.7	387
17.0	62.6	514	27.0	80.6	440	37.0	98.6	384
17.5	63.5	509	27.5	81.5	438	37.5	99.5	381
18.0	64.4	505	28.0	82.4	435	38.0	100.4	378
18.5	65.3	501	28.5	83.3	432	38.5	101.3	374
19.0	66.2	497	29.0	84.2	429	39.0	102.2	371
19.5	67.1	493	29.5	85.1	427	39.5	103.1	368
20.0	68.0	489	30.0	86.0	424	40.0	104.0	365

TABLE III

C.cm. of stock copper sulphate solution of gravity 1.1000. to be diluted to 100 c.cm., 50 c.cm. or 25 c.cm. to prepare standard solutions of gravity, G. to within ± 0.0001

G.	100	50	25
1.008	7.33	3.67	1.84
9	8.32	4.16	2.08
10	9.31	4.66	2.33
11	10.30	5.15	2.58
12	11.29	5.65	2.83
13	12.28	6.14	3.07
14	13.27	6.64	3.32
15	14.26	7.13	3.57
16	15.25	7.63	3.82
17	16.24	8.12	4.06
18	17.23	8.62	4.31
19	18.22	9.11	4.56
20	19.21	9.61	4.81
21	20.20	10.10	5.05
22	21.19	10.60	5.30
23	22.17	11.09	5.56
24	23.15	11.58	5.79
25	24.14	12.07	6.04
26	25.12	12.55	6.28
27	26.10	13.05	6.53
28	27.08	13.54	6.77
29	28.06	14.03	7.02
30	29.04	14.52	7.26
31	30.0	15.01	7.51
32	31.0	15.50	7.75
33	32.0	16.00	8.00
34	33.0	16.50	8.25
35	34.0	17.00	8.50
36	35.0	17.50	8.75
37	36.0	18.00	9.00
38	37.0	18.50	9.25
39	38.0	19.00	9.50
40	39.0	19.50	9.75
41	40.0	20.00	10.00
42	41.0	20.50	10.25
43	42.0	21.00	10.50
44	43.0	21.50	10.75
45	44.0	22.00	11.00
46	45.0	22.50	11.25

G. = specific gravity of standard solution.

100 = c.cm. of 1.100 stock solution diluted to 100 c.cm.

50 = c.cm. of 1.100 stock solution diluted to 50 c.cm.

25 = c.cm. of 1.100 stock solution diluted to 25 c.cm.

SEROLOGICAL TECHNIQUE

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CONSTITUTION OF BLOOD

Blood = Formed structures (red corpuscles, white corpuscles and platelets) + plasma.

Plasma = Fibrin + serum (separating on clotting).

Serum = Serum albumin + serum globulin + metabolic products + salts + water.

Serum globulin = Pseudoglobulin + euglobulin.

EXPLANATIONS AND DEFINITIONS

A SUBSTANCE which after a parenteral (other-wise than through *enteron*, intestine) entry into a living body produces in the body anti-

substances which react with the substance is an antigen. The anti-substance is an antibody which is found in the blood, plasma or serum and is contained in the serum globulin.

Serological reactions are antigen-antibody reactions. They are also called immunological reactions or biological reactions. The serological technique sets up these reactions. It is also employed frequently in bacteriology with a slight variation.

The following are not serological, immunological or biological reactions: (1) Analysis of serum for sugar, urea, etc., although the material tested is serum. (2) Detection of hormones in pregnancy and morbid states, although a living animal is used in the process. (3) Testing of toxins for potency on animals. (4) Testing of antitoxins for potency on animals which are under the influence of toxins. These are protection experiments. (5) Certain skin tests which depend on the presence or absence of antitoxins which neutralize toxins used in the test. They are also protection experiments.

Reactions of allergy involving skin and deeper tissues, on the other hand, come under serological reactions.

This series of communications will deal with common immunological procedures employed in hæmagglutination, precipitin reaction, complement fixation and reactions of allergy.

A reaction becomes a test when completed and interpreted. The two terms, *reaction* and *test*, are, therefore, employed interchangeably very frequently.

SPECIAL FEATURES OF SEROLOGICAL TECHNIQUE

Sterility.—Unlike bacteriological procedures serological procedures cannot be carried out in perfect sterility. The apparatus is sterile, the manipulations are carried out with care and the reagents, before and after the reaction, are preserved mainly by the action of cold of various degrees in a refrigerator. (The ice box is rather a poor substitute.) Antiseptics are permissible at times. During the manipulation a sterility approaching *surgical sterility* can and should be maintained.

Speed.—The reactions are *timed*, the manipulations are of the nature of a *drill*.

Accuracy of measurement.—Measurements must be carried out and quantities delivered without delay. Chemical accuracy is neither possible nor necessary. In preparing chemical solutions used in the serological procedures, however, the chemical accuracy is preserved.

Temperature.—Temperatures are very important. Certain steps are carried out at certain temperatures only. Water baths and incubations are necessary.

Dilutions.—Dilutions and suspensions of the reagents used, recorded and spoken of are *initial* dilutions, unlike the dilutions of the antisera used in bacteriology, which are *ultimate* dilutions.

Dose.—The volumes of the dilutions used are kept constant. (Any convenient volume for a particular type of reaction, from a drop specially measured to 0.25 c.c., will suffice.) The dose, therefore, can be varied by varying the strength of the dilution. The strength of the dilution, therefore, is the dose. This is unlike what occurs in posology in which a weighed or measured quantity is the dose (this point will be made more clear in the description of the titre of the hæmolytic amboceptor and the serum complement).

HÆMAGGLUTINATION

Effect on rbc of foreign plasma.—Generally plasma (or serum) of an animal of one species clumps together, agglutinates, the rbc of an animal of another species. In the rbc there is an antigen, the hæm(agglutin)ogen, which is acted upon by naturally existing (not arising as a result of parenteral entry of the antigen) antibody, the hæm(agglut)inin. The action makes the surface of the rbc sticky: hence the clumping. The clumping is the hæmagglutination. (The meaning of the convenient term hæmogen used in this connection is different from what it may have in pharmacology, as a 'normal' salt solution in physiology is different from the one in chemistry.)

Effect of plasma or serum of the same species.—An agglutination, when it occurs, is iso-hæmagglutination brought about by: (1) Two iso(hæmagglutino)gens A and B present in the rbc and two iso(hæmaggluti)nins a and b (usually called α and β for no reason at all) present in the plasma A-containing rbc are agglutinated by a and B-containing rbc are agglutinated by b. Some subjects' rbc contain neither A nor B, while others' contain both A and B. The four possible combinations compatible with life are the four blood groups (see figures 1 and 2, plate XXI). (2) Hæmogens M and N, possibly. (3) Rh hæmogens. (4) Hæmogen P, etc. (5) Cold agglutinins.

EXPLANATION OF FIGURES 1 AND 2, PLATE XXI

A and B are the isogens.

a and b are the corresponding isonins. In figure 2, a fits A, b fits B, and both fit AB, binding the discs (= hæmagglutination), while neither fits O.

The group is named after the isogen.

The four groups indicate the only four possibilities, compatible with life, in which the isogens and the isonins can co-exist in the same subject. In a 'defective' group an isonin which can exist compatibly with life is absent (e.g. O, a; A, o).

Further division of A into A_1 and A_2 (and into A_1B and A_2B) increase the number of groups to six.

Old equivalents of the new nomenclature are:—

NEW	Jansky	OLD
O	I	Moss
A	II	IV
B	III	II
AB	IV	III
		I

Effect of a subject's own plasma.—An agglutination when occurring is autoagglutination.

Special apparatus, chemicals, etc., used in hæmagglutination (see figures 3 and 4, plate XXI): 1. **Moist chambers.**—They are made from medium-sized petri dishes by enclosing in each a watch glass containing a folded filter paper dripping with water. The watch glass may be secured in place near the rim by plasticine. A wet open preparation on a slide in such a chamber does not dry up.

2. **Microscope slides.**—Old slides which have been in use for a year or so for other procedures are preferable to new ones on which drops of rbc suspension do not spread evenly. When two or more tests are done on the same slide the obverse is partitioned by lines drawn with a glass marking pencil. Distinctive marking or writing is put on the reverse and *along the lower border* of the slide (to decide at a glance, later, if the slide is lying with the right edge up). The writing on the reverse although executed from under the slide should not be laterally inverted when seen from above. Four slides (and a watch glass) can be managed with perfect ease in a moist chamber.

3. **Calibrated capillary teat pipettes and finger pipettes.**—Their points fit the hole no. 58 of the wire gauge of L. S. Starrett and Co., U.S.A., and deliver 50 drops to 1 c.c. (A single disc with the same hole can be obtained from the Mathematical Instrument Department of the Survey of India, Calcutta.)

The pipettes in suitable containers are sterilized by autoclaving. (The teat pipettes—without the teats—are wrapped individually in brown paper and then put in a metal cylinder plugged with cotton-wool. The finger pipettes are held unwrapped in a large test-tube with cotton-wool at the bottom.) With a suitable tilt a finger pipette picks up many drops of fluid. The movement of the rising fluid is helped by opening and closing rapidly the upper end with the finger. Drops are delivered with the pipette upright.

For measuring drops of whole blood (mostly for field work) the finger pipettes are dipped in 3 per cent sodium citrate solution which is allowed to dry inside. They are then sterilized in the same way.

Some pipettes are prepared with a cotton-wool plug at the upper end. With these fluids are taken from sterile stocks preserved in the refrigerator.

It is a pity these pipettes are not in common use. Nearly all the errors, difficulties, differences of opinions and biases in hæmagglutination are due to the difficulties of quick, accurate and repeatable measurements such as these pipettes ensure.

The pipettes, after use, can be dropped in a tall cylinder containing sand or glass wool at the bottom and cleaned for further use. The point will need inspection.

4. *Glass rods with rounded ends.*—For mixing rbc with fluids on a slide these rods are indispensable.

5. *Cleaning of glassware.*—(1) Preliminary wash in running water. (2) Submersion in 10 per cent hydrochloric acid for a night in a glazed jar. (3) The fluid in the jar after the glassware has been submerged should effervesce on a stone. The acid digests all remains of blood. The glassware should be crystal clear on inspection. (4) Submersion in running water for an hour. Testing water for acid reaction. (5) Submersion in distilled water. (6) Change of distilled water. Testing with silver nitrate for remains of tap water. (7) Jerking free of

and in a good state of preservation. The coarse particles are rejected after they have settled down and the suspension washed twice.

From the final deposit make a 2 per cent suspension thus : (1) Measure and deliver into a tube 1 c.c normal saline with an ordinary graduated pipette. (2) Remove from the tube 1 drop with the calibrated teat pipette. (3) Add to the tube 1 drop of washed rbc deposit with the same teat pipette. (4) Shake to make a homogeneous suspension. (1 drop in 50 drops = 2 drops in 100 drops = 2 per cent.)

Setting up tests : 1. *For unknown rbc.*—Make a 2 per cent suspension and add to the known sera, thus :

With potent sera

Known a	Unknown	Known b	Unknown
1 drop	+ suspension 1 drop	1 drop	+ suspension 1 drop

With indifferent sera

Known a	Unknown	Known b	Unknown	Known ab	Unknown
1 drop	+ suspension 1 drop	1 drop	+ suspension 1 drop	1 drop	+ suspension 1 drop

water. (8) Drying on racks. (9) Drying in oven. (10) Sterilizing in autoclave or oven (without cotton-wool plug most pieces, with plugs certain pieces only). Sand and glass wool are cleaned in the same way.

DETERMINATION OF THE GROUP OF BLOOD

Testing sera and testing rbc : 1. *Known serum a (from subject B) and known serum b (from subject A).*—They should in a dilution of 1 in 5 agglutinate known rbc A and known rbc B almost immediately and should not affect known rbc O (*vide infra*, anti-O serum). If such potent sera are not available, a serum ab (from subject O) should also be included : isonins a and b in a serum ab are on the whole stronger than those occurring individually.

The sera are used undiluted.

2. *Known rbc A and known rbc B.*—The rbc should agglutinate readily and well. All samples of rbc A are not satisfactory for this purpose (*vide infra*, 'slow' A and A₂). The known blood is taken in a test-tube containing an equal or a greater volume of citrated saline (normal saline containing 1.5 per cent sodium citrate) and washed thus : (1) Centrifuge the tube (for 5 to 7 minutes). The rbc fall as a deposit to the bottom leaving the slightly straw coloured plasma, diluted with saline, supernatant. (2) Pour off the supernatant fluid, add saline, shake, centrifuge again. Obtain the deposit. This is the first washing. For tests and experiments the rbc are washed three times.

From blood taken for other purposes (*e.g.* the Wassermann reaction) rbc can be washed out of the divided clot in saline if the clot is fresh

Mix with the special rod (one end for each mixture) and spread over an area about 1.5 cm. in diameter. Place in moist chamber. Hold the moist chamber in both hands and move quickly in a small circular orbit, clockwise and then counter-clockwise, with an up and down tilt. Impart a side to side movement off and on. These movements (i) make the suspension of blood uniform in the first instance, (ii) help in hæmagglutination later, and (iii) aid the eye in the end, the agglutinated masses of rbc becoming easier of detection on movement.

Examine immediately and then every 15 minutes for $\frac{1}{2}$ hour (without removing the slide from the moist chamber). Record result at the end of $\frac{1}{2}$ hour under each compartment, drawn on the paper, according to the following notation :

Rbc agglutinated in clumps which have moved to the periphery of the preparation (agglutination centrifugal)	..	++
Rbc agglutinated in clumps which have remained where they formed or have moved to the centre on rotating the slide (agglutination centripetal)	..	+
Intermediate	..	+ (+)
Granularity only	..	±
Suspension as it was	..	—
++ clumps sometimes become large plaques and move centrally. They are best recorded as	..	++
± is not likely to be encountered with potent sera.		

If only a agglutinates, the unknown rbc are A
If "b" neither a nor b agglutinates, the unknown rbc are O.
If both a and b agglutinate, the unknown rbc are AB.

A suspension agglutinated by serum ab is not of rbc O even if the indifferent testing sera appear to leave it untouched.

In figure 4, plate XXI, slides 1, 2, 3 and 4 indicate groups O, A, B and AB respectively.

2. For unknown serum.—Add undiluted unknown serum to the 2 per cent suspensions of the known rbc, thus :

Known suspension	Unknown serum	Known suspension	Unknown serum
A + 1 drop	B + 1 drop	A + 1 drop	B + 1 drop

Mix, spread, watch and read as before

If the serum agglutinates suspension A only, it is a.
 " " " " " B " " b.
 " " " " " both A and B " " ab.
 " " " " " neither A nor B " " o*.

* Serum o comes from sub-group AB.

In figure 4, plate XXI, if the slides were prepared with known rbc for identifying the unknown sera, slides 1, 2, 3 and 4 would indicate groups AB, B, A and O respectively.

The rbc and serum from the subject under examination must agree. When they do not agree an explanation must be found (*vide infra*).

A \pm reaction or even an unexpected — reaction is possible. Double the dose of the serum and observe again. If the expected reaction of an isonin is not seen the isonin is absent and the group is defective. The writers, however, have not yet found a defective group. An extremely weak reaction is likely to turn negative if the serum is weakened by an extra drop of saline as has been advised by most previous workers. The extra drop of saline is supposed to guard against the action of cold agglutinins (*vide infra*). It is not necessary.

Theoretically a zone phenomenon is possible : an undiluted serum not agglutinating the rbc may do so on dilution. The writers have never seen such an occurrence.

The technique so far described employs slides only. The rbc and sera can be tested in small test-tubes also as is done routinely for Rh incompatibility (*vide infra*). For determining the group of blood there is no advantage in using tubes.

Universal donor.—Rbc O having no affinity (no receptor) for either of the two isonins cannot be agglutinated by any recipient : hence the term 'universal donor'. But the isonins in a donor O, if strong enough, can kill recipients of all other groups. The writers term O donors 'safe universal donors, 1st quality', if their sera do not agglutinate 2 per cent rbc A and rbc B in a 1 in 16 initial dilution; and 'safe universal donors, 2nd quality', if their sera just agglutinate rbc A and rbc B in 1 in 16 but not in 1 in 50. No more than 200 c.c. of blood may be transfused into an adult from a safe universal donor of 2nd quality. Other 'universal donors' are 'dangerous'.

Rbc O will not suit some recipients A₁ and A₂B (*vide infra*).

An older standard is that a 1 in 9 dilution of the donor's serum should not agglutinate an equal volume of the recipient's rbc in a 50 per cent suspension.

Universal recipient.—Subjects AB having no isonins in their blood cannot agglutinate rbc of any donor : hence the term 'universal recipient'. But they can be killed by donors of all other groups with strong enough isonins. For safety, donors of all other groups for recipients AB should satisfy the same conditions as the universal donor for other groups.

The Sub-groups

Isogen A is divisible into A₁ and A₂ (A₂ described a few years ago has not survived).

The four groups thus become six :—

O, A₁, A₂, B, A₁B and A₂B.

A₂ and A₂B are less frequent than A and AB.

Determination of A₂.—Take 2 c.c. serum a (from subject B) and divide into two equal parts. To one part add an equal volume of a deposit of washed rbc suspected to be A₂ (by slowness and/or weakness of reaction), shake into suspension, and leave at room temperature $\frac{1}{2}$ hour, in the cold $\frac{1}{2}$ hour and at room temperature again $\frac{1}{2}$ hour. Centrifuge to remove the supernat, the absorbed serum a. It will not agglutinate another sample of the same (suspected rbc): yet it will agglutinate ordinary (unsuspected) rbc A, if the suspicion is well founded. The suspected A is A₂. Any other sample of rbc A reacting with the unabsorbed serum but not with the absorbed serum will also be A₂.

Unusual Reactions associated with Sub-groups

Sera of some subjects A₁ and A₁B.—They are known to agglutinate rbc A₂, rbc A₂B and rbc O. They are a₂ sera or anti-O sera. Anti-O sera is a better description in as much as such sera agglutinate all rbc O without exception.

Sera of some subjects A₂ and A₂B.—Conversely to the last occurrence they agglutinate rbc A₁ and rbc A₁B.

Other Unusual Reactions

These reactions are : (1) Intra-group reaction in group B. (2) Agglutination of rbc O by sera other than a₂. (3) Agglutination caused by serum o (from subject AB).

Cold Agglutinins

Isonins against otherwise compatible rbc exist but are operative in the cold only. At body temperature they are inert but may be activated to act at room temperature by a previous transfusion of the appropriate (susceptible) rbc.

Auto-agglutinins

They are probably cold agglutinins which become active due to an abnormal interference by a transfusion or to a morbid process.

Bacteriogenic Agglutination

Old rbc agglutinate on the addition of human serum, independent of the isonins. An enzyme produced by bacteria acts on the rbc and

activates a latent antigen T. Anti-T agglutinins are present normally in all human sera : hence the agglutination. Bacterial agglutination is also called pan-agglutination.

Pseudo-agglutination

This semblance of isoagglutination is produced by three causes : (1) Rouleaux formation due to the action of some sera, including the sera of some recipients. Under the microscope rouleaux can be seen in the clumps. (2) Wharton's jelly in the umbilical cord blood sera. When the slide is moved the rbc form clumps which break up when the slide is at rest. (3) Coagulation of plasma in unwashed or inadequately washed rbc. In anæmic states recipient's unwashed or inadequately washed rbc sometimes cause this complication. The coagulation can be distinguished from agglutination.

Cross-matching for Transfusion of Blood

When the donor and the recipient belong to the same group.—

(i) For rbc and sera

Donor's rbc, 2% + 1 drop	Recipient's serum 1 drop	Recipient's rbc, 2% + 1 drop	Donor's serum 1 drop
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There should be no hæmagglutination as a rule. As an exception, intra-group hæmagglutination occurs because of : (1) The abnormal isonins occurring in sub-groups of A. The reaction between 2 subjects A should be watched with particular care, especially after a previous transfusion of blood. (2) Rh incompatibility (*vide infra*). (3) Type incompatibility (*vide infra*). (4) Pregnancy, some cases. (5) Morbid state in the recipient. (6) Iso-immunization with other hæmogens after a previous transfusion.

For second and subsequent transfusion in males and even first transfusion in married females (for reasons connected with pregnancy) Rh incompatibility is specially important. The reaction with the recipient's serum should also be tested in a small test-tube (WR tube) thus : (1) Mix recipient's serum 3 standard drops with 2 per cent suspension of donor's rbc 3 standard drops. (2) Incubate at blood heat 1 hour. (3) Store in the cold 1 hour (to allow the rbc to settle down). (4) Examine the deposit over the concave mirror of a microscope lying on its side (*vide Rh*).

(ii) For sera only

Donor's serum 1 drop	Recipient's serum 1 drop	Donor's serum 2 drops	Recipient's serum 2 drops
----------------------------	--------------------------------	-----------------------------	---------------------------------

(1)

(2)

(3)

There should be no increase in opalescence in (1) unless an increase is seen in (3) also, due to change in the recipient's serum on exposure. (2) is a control of a double volume of serum

for comparing appearances. It should not become opalescent on exposure.

The increase in opalescence in (1) only will be due to causes other than those falling under isohæmagglutination, other immunological reactions which must be avoided. For this purpose a scratch test may also be done on the recipient with the donor's serum. If time permits a complement-fixation test between the two sera may also be undertaken. (Recipient's serum, 1 in 5, 1 vol. + donor's serum, 1 in 5, 1 vol. + guinea-pig complement 2 HMD in 1 vol. . . . room temperature $\frac{1}{2}$ hour and incubation $\frac{1}{2}$ hour . . . sensitized sheep rbc 1 vol. . . . incubation $\frac{1}{2}$ hour = complete hæmolysis. Serum controls will be necessary. Recipient's serum may be anti-complementary in which case an allowance for more complement must be made. The donor's serum must not be anti-complementary. *Vide infra*, under complement fixation).

When a universal donor is used.—Only the rbc of the donor will not (ordinarily) be agglutinated by the serum of the recipient. The opposite combination is bound to produce hæmagglutination (isonins a and b + rbc of any group other than O = hæmagglutination).

When a universal donor is being used for a recipient O, it is not being used as a universal donor but as a donor O.

Making of dilutions of sera for testing safety of donors

1. One in 50 dilution. Measure into a test-tube 1 c.c. of saline. Remove 1 standard drop. Add 1 standard drop of the serum under test and shake. Use 2 drops for testing. Discard 2 drops, leaving 46 drops in the tube.

2. One in 16 dilution. To the balance left in the tube add 2 standard drops of serum. Ignoring the small quantity of the serum removed previously there will now be 3 drops of serum in 48 drops of the total fluid. This is, for all practical purposes, equal to a 1 in 16 dilution.

3. One in 9 dilution. For performing the single and simple test needing the dilution accuracy is employed. To 8 standard drops of saline add 1 standard drop of serum.

For second and subsequent transfusion in males and even first transfusion in certain females guard against Rh incompatibility and use tubes also as before.

When a donor other than AB is used for a universal recipient.—Only the serum of the recipient will not (ordinarily) agglutinate the rbc of the donor. The opposite combination is bound to produce hæmagglutination. (Isogens AB + isonins a and/or b from any group other than AB = hæmagglutination.) The serum of the donor, therefore, must satisfy the standards laid down for a safe universal donor (*vide supra*).

Guard against Rh incompatibility as before.

To be continued.

A SIMPLE METHOD OF ESTIMATING THE TITRE OF KAHN ANTIGEN

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and

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OF all the various precipitation tests for syphilis that have been described, Kahn standard test has come to be adopted as the precipitation test of choice in most laboratories. To secure uniformity of sensitivity and specificity of the reaction, many important details have to be adhered to, of which the preparation of the antigen, finding the correct titre and adjustment for sensitivity of the antigen, if found necessary, are stressed by the author of the test.

According to the method adopted by Kahn (Ref. Serum diagnosis of syphilis by precipitation by R. L. Kahn) for the determination of the titre, the precipitated particles that have to be looked for in the tubes are so minute that it needs much experience to detect them. The fine precipitate is also sometimes associated with cholesterol crystals which are likely to cause some confusion. Very often difficulty is therefore experienced in judging the correct titre. A modified and simpler method has been described in this note for arriving at the correct titre. The results obtained by this method are in agreement with those that are obtained by the usual method.

The method is briefly described below :—

One c.cm. of antigen is measured into one row of Kahn antigen vials in the rack. Varying amounts of saline 0.9 c.cm., 1.0 c.cm., 1.1 c.cm., 1.2 c.cm., 1.3 c.cm., 1.4 c.cm., etc., are measured into the opposite row of vials. The antigen and saline are mixed together as described in Kahn's technique, six times as quickly as possible without caring to drain the tubes completely. The saline is added to the antigen first. The rack is kept aside for ten minutes. The vials are then inspected with the naked eye for the appearance of the mixtures and disposition of the aggregates in the mixture. In the vials containing lesser amounts of saline, viz, 0.9 c.cm., 1.0 c.cm., the aggregates are fine and tend to accumulate at the bottom of the vials with the result that an almost clear supernatant layer with very few suspended aggregates can be made out. There is also a fine layer of froths and aggregates at the top of the antigen suspension in every vial.

In the vials that contain larger amounts of saline, viz, 1.1 c.cm., 1.2 c.cm., the aggregates are larger in size and tend to be suspended in the medium so that there is no clearing of fluid between the top and bottom layers, as compared with the vials containing lesser amounts of saline. In the vials, containing still larger amounts of saline, viz, 1.3 c.cm., 1.4 c.cm., the

aggregates are suspended in almost the whole of the medium which appear homogeneous. The particular vial where the aggregates are suspended in the form of vertical strands joining the top and bottom layers of aggregates is taken as the titre. In the next vial the aggregates tend to disintegrate and become homogeneous in the fluid. The appearance of the vials after 10 minutes is shown in the adjoining photograph (see figure on plate XXII). The arrow in the photograph points to the titre. The titres of a number of over thirty batches of Kahn standard antigen arrived at by this method and Kahn's original method were identical (see table).

In some cases, two adjoining vials may show similar appearance so that some difficulty may arise as to which tube should be taken as pointing to the titre. An inspection with a hand lens will help to clarify this and it is usually found that the higher dilution of the two is the correct titre.

TABLE

Date	Titre by the new method	Titre according to Kahn's technique
16-7-44	1.2	1.2
30-7-44	1.2	1.2
8-9-44	1.3	1.3
23-10-44	1.2	1.2
9-12-44	1.3	1.3
17-1-45	1.3	1.3
19-1-45	1.3	1.3
25-1-45	1.2	1.2
28-1-45	1.2	1.2
24-2-45	1.3	1.3
27-2-45	1.3	1.3
23-3-45	1.3	1.3
27-3-45	1.3	1.3
30-4-45	1.3	1.3
2-5-45	1.3	1.3
2-6-45	1.3	1.3
4-6-45	1.3	1.3
7-7-45	1.2	1.2
9-7-45	1.2	1.2
30-7-45	1.3	1.3
1-8-45	1.3	1.3
7-9-45	1.3	1.3
11-9-45	1.3	1.3
10-10-45	1.3	1.3
14-11-45	1.2	1.2
5-12-45	1.2	1.2
2-1-46	1.2	1.2
11-1-46	1.3	1.3
8-2-46	1.3	1.3
6-3-46	1.3	1.3
6-4-46	1.2	1.2

EPITROCHLEAR GLANDS

A STUDY IN 50 CASES

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ONE of the valuable signs of syphilis is believed to be palpable epitrochlear glands. During the primary stage of the disease a week or so after the local lymph glands have begun to enlarge there is universal adenitis, which can be appreciated by palpation, particularly of the

epitrochlear, axillary and cervical glands (Harrison, 1946). There are other diseases apart from syphilis in which these glands enlarge and become palpable. They are lymphatic

The present work was undertaken to assess the value of palpable epitrochlear glands in the diagnosis of syphilis. From among the patients admitted to the Thomason group of hospitals

TABLE

Number	Name	Age, race and sex	Disease for which admitted	Size of epitrochlear glands	W.R
1	M. K.	10, M. M.	Rheumatoid arthritis	+++	---
2	R.	8, H. M.	Scrofula	++	---
3	B.	10, H. F.	Portal cirrhosis	++	---
4	B. D.	20, H. M.	Influenza	+++	---
5	H. A. K.	50, M. M.	Polyserositis	++	---
6	H. R.	25, M. M.	Bengal splenomegaly	+++	---
7	K. A.	60, M. M.	Syphilis of the stomach	+++	+++
8	U. K.	25, M. M.	Abdominal tuberculosis	+	---
9	D.	18, H. M.	Spinal caries	+	---
10	G. L.	50, H. M.	Heart failure	++	---
11	H. K.	30, M. M.	Bengal splenomegaly	+	---
12	B. S.	32, H. M.	Chronic malaria	++	---
13	K. A.	15, M. M.	Nephritis	+++	---
14	S. R.	50, H. M.	Portal cirrhosis	++	---
15	A. S.	14, H. M.	Generalized adenitis	+++	+++
16	R. S.	25, H. M.	Arthritis	+++	---
17	K. S.	10, H. M.	Typhoid fever	++	---
18	A.	9, M. F.	Epilepsy	+	---
19	P.	9, H. F.	Chorea	++	---
20	T.	10, H. F.	Chronic malaria	+	---
21	M.	50, H. F.	Corrosive poisoning	+	---
22	B.	28, H. F.	Acholic jaundice	+	---
23	G.	18, H. F.	Pulmonary tuberculosis	++	---
24	S. D.	26, H. F.	Heart failure	+	---
25	M. B.	15, H. F.	Epilepsy	+	---
26	A. D.	28, H. F.	Pulmonary tuberculosis	+	---
27	B.	15, H. F.	Hemiparesis	++	---
28	B.	30, H. F.	Nephrosis	+++	+++
29	C.	58, H. F.	Cancer liver	++	---
30	R.	7, H. M.	Paraplegia	+++	---
31	P.	9, H. F.	Chorea	+++	---
32	R.	30, H. F.	Pulmonary tuberculosis	++	---
33	C.	25, H. F.	Amoebic hepatitis	++	---
34	K.	18, H. F.	Abdominal tuberculosis	+++	---
35	K. F.	16, M. F.	Abdominal tuberculosis	++	---
36	C. L.	18, H. M.	Chronic malaria	+	---
37	B. D.	22, H. M.	Arthritis	+	---
38	T. D.	46, H. M.	Myxœdema	++	++-
39	R.	11, H. F.	Myopathy	+++	---
40	N. S.	22, H. M.	Pleurisy with effusion	+++	---
41	N. L.	35, H. M.	Double mitral and aortic incompetence.	++	---
42	C. L.	35, H. M.	Ankylostomiasis	++	---
43	N. B.	50, H. M.	Hemiplegia	+++	---
44	K. L.	56, H. M.	Hemiplegia	+++	---
45	R.	16, H. M.	Encephalitis	++	---
46	A. S.	42, H. M.	Bronchitis	+++	---
47	R. B.	45, H. M.	Sub-acute combined degeneration.	++	---
48	S. S.	18, H. M.	Abdominal tuberculosis	++	+ --
49	T. B. M.	46, Ch. M.	Typhoid fever	++	---
50	V. P. G.	30, H. M.	Neurosis	++	---

Age is given in years.

H. M. = Hindu male.

M. M. = Muslim male.

Ch. M. = Christian male.

H. F. = Hindu female.

M. F. = Muslim female.

leukaemia, Hodgkin's disease, Still's disease, local septic infections, etc. Barring septic infection the other diseases are comparatively rare. Hence importance has fallen on syphilis as the cause of palpable epitrochlear glands.

attached to the Agra Medical College, those were chosen who had palpable epitrochlear glands. The results are given in the table. In the appended table the diseases for which they were admitted have been mentioned. The size

of the glands has been graded as one, two and three plus. One plus means just palpable, two mean moderate enlargement and three mean fair degree of enlargement. In all the cases the glands were palpable on both sides. In each case the W.R. of blood was done to find out how many were syphilitic and how many non-syphilitic.

Conclusions

Among 50 cases with palpable epitrochlear glands, W.R. was positive in 5 (10 per cent). Case no. 7 was proved to be syphilitic by therapeutic test; nos. 15, 28 and 38 gave definite history of acquired syphilis. To no. 48 whose W.R. was suspicious, \pm — —, was given a provocative injection, and his W.R. became positive (+ — —) although he denied having had any exposure. In 45 cases (90 per cent) with palpable epitrochlear glands the W.R. was completely negative. None among them gave any history of syphilis nor of having received any treatment, which might point towards it. The present work proves that palpable epitrochlear glands do not invariably mean syphilis. As a matter of fact, a large bulk of non-syphilitics have palpable epitrochlear glands. It seems that the value of this sign in the diagnosis of syphilis has been over-estimated.

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NORMAL INTRAPLEURAL PRESSURES AMONG INDIANS

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THE present work consists of the measurement of normal intrapleural pressures among Indians. Fifty patients were chosen among whom 40 were males and 10 females. Every patient before being selected, was examined clinically and radiologically to exclude diseases of the lungs, the heart and also any debilitating state which might interfere with the intrapleural pressures. The Modified Lillingston and Pearson Pneumothorax apparatus was used. The site chosen was the sixth space in the anterior axillary region either on the right or the left side. The results are tabulated below.

TABLE

Number	Name	Age, race and sex	Intrapleural pressure in cm. water	Mean pressure in cm. water
1	S. C. T.	40, H. M.	-6, -4	-5
2	B. T.	13, H. M.	-6, -2	-4
3	L.	24, H. M.	-12, -8	-10
4	R. S.	30, H. M.	-7, -6	-6.5
5	B. K.	27, H. M.	-8, -5	-6.5
6	R. B.	45, H. M.	-6, -4	-5
7	C.	70, H. M.	-8, -6	-7
8	S. P.	56, H. M.	-14, -10	-12
9	B. P.	23, H. M.	-10, -6	-8
10	R. S.	45, H. M.	-10, -6	-8
11	H. P.	30, H. M.	-10, -7	-8.5
12	B. N.	50, H. M.	-10, -8	-9
13	B. D.	40, H. M.	-7, -4	-5.5
14	S. S.	18, H. M.	-8, -4	-6
15	J.	18, H. M.	-12, -6	-9
16	D.	60, H. M.	-3, -1	-2
17	B. L.	40, H. M.	-10, -6	-8
18	N. K.	50, H. M.	-12, -6	-9
19	R.	14, H. M.	-10, -2	-6
20	N.	45, H. M.	-10, -5	-7.5
21	M. S.	30, H. M.	-9, -4	-6.5
22	G.	28, H. M.	-10, -2	-6
23	R. D.	20, H. M.	-8, -4	-6
24	R.	30, H. M.	-12, -4	-8
25	N. R.	20, H. M.	-12, -4	-8
26	H. C.	20, H. M.	-11, -4	-7.5
27	G. S.	55, H. M.	-4, 0	-2
28	A. K.	19, H. M.	-7, -1	-4
29	R. P.	18, H. M.	-4, 0	-2
30	K.	25, H. M.	-7, -1	-4
31	S. L.	38, H. M.	-14, -2	-8
32	B. D.	45, H. M.	-10, -3	-6.5
33	C. S.	35, H. M.	-12, -1	-6.5
34	C. B.	42, H. M.	-11, -4	-7.5
35	M. L.	36, H. M.	-12, -3	-7.5
36	R. S.	30, H. M.	-12, -6	-9
37	B. L.	64, H. M.	-7, -3	-5
38	K. L.	30, H. M.	-10, -6	-8
39	S. S.	30, H. M.	-11, -5	-8
40	L.	28, H. M.	-12, -6	-9
41	R. D.	30, H. F.	-6, 0	-3
42	P.	17, H. F.	-7, -1	-4
43	S. D.	20, H. F.	-7, -2	-4.5
44	M.	40, H. F.	-8, 0	-4
45	R. K.	35, H. F.	-8, -1	-4.5
46	I. D.	65, H. F.	-13, -2	-7.5
47	R. D.	40, H. F.	-8, -3	-5.5
48	K.	25, H. F.	-14, -2	-8
49	R. P.	60, H. F.	-9, -2	-5.5
50	K.	25, H. F.	-10, -5	-7.5

H. M. = Hindu male.

H. F. = Hindu female.

Conclusions.—It is concluded that the normal intrapleural pressures among Indians is -14 to -3 cm. water during inspiration, -10 to 0 cm. water during expiration, and the mean pressure is -12 to -2 cm. water.

My thanks are due to Major-General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S. (retd.), Principal, Medical College, Agra, for his kind permission to publish this work; to Drs. H. S. Prasad, B. B. Sharma, R. S. Gupta, M. N. Kapur, B. K. Sharma, B. B. L. Mathur and U. C. Jain, and to the nursing staff.

[Note.—The normal negative pressure of English writers is '5 to 10 or more cm. of water', *Textbook of Practice of Medicine*, F. W. Price, fifth edition, 1937.—Error, I.M.G.]

ORAL SEPSIS AND ITS RELATION TO NERVOUS DISORDERS

By ARUN GANGULI, Z.D.S. (Vienna), F.D.I.

Chief Dental Surgeon, Gwalior State

AMONG the nervous disorders attributable to mouth infection are: neuralgia, tic douloureux, mental depression, dizziness, insomnia, headache (frontal, vertical and occipital), painful spine, Bell's palsy and psychoses due to debilitating anæmias as a result of long-standing toxic absorption. Infected teeth, in addition to micro-organisms, contain toxic substances and it is possible that mouth infection causes a state of anaphylactic sensitization which may disappear upon the removal of the teeth.

Neuralgia

A large proportion of the sensory-nerve disturbances of the mouth are attributable to referred pain arising from terminal nerve irritation in the teeth, gums, tongue, or mouth. This terminal irritation produces referred pain in another area in the mouth or in one of the facial areas. The neuralgic pain is intermittent and usually diffuse and ill defined. There may be tenderness or painful localized sensation. The pain may be slight but in many cases very violent, which generally radiates behind the ear, above the eyebrow, in the ear, over edge or below the eye, or in the mental region. Before the onset of the pain there may be uneasy sensation sometimes tingling in the part which will be affected. The pain is localized to a certain group or division of nerves, usually affecting one side. It is not constant, but paroxysmal and is described as stabbing and burning in character. After lasting a variable time, from a few minutes to many hours, the attack subsides. Recurrence may be at definite intervals every day at the same time or at intervals of 2, 3, or even 7 days. The skin may be exquisitely tender in the affected region, particularly over certain points along the course of the nerve, the so-called tender points. Movement as a rule is painful. The prognosis of this type of neuralgia in most cases is very good as the neuralgia usually disappears after removal of the local cause. In a small percentage of cases it may be impossible to eliminate the exciting cause such as persistent otitis of the jaw where sclerosis has occurred; then the only permanent cure is by surgery of the nerve.

Case history.—Mrs. P., Hindu widow, aged 45, suffered from terrible neuralgic pain of the right side of the face for over 3½ years. Pain used to come at definite intervals and last variable time. Local treatment was of no or very little effect. Examination of the mouth showed the following conditions:—

Gums of both upper and lower jaw bad. Smear from gum shows numerous pus cells, fair amount of epithelial cells, Vincent's spirilla and fusiform bacillus.

On culture blood agar plates showed *Streptococcus viridans* with a few colonies of *Staphylococcus albus*.

Teeth.—Exposed cementum in upper right lateral canine and second premolar. Those 3 teeth were extremely sensitive to touch.

X-ray of the teeth and antrum showed no more abnormalities. The skin over the affected area was exquisitely tender particularly along the course of the nerve. The movement of the muscle was painful. The skin over the area was hot. The patient was restless and irritable.

At my first visit the upper right, 2nd, 3rd, and 5th molars were extracted under local anaesthesia. I was informed next day that the stabbing pain had disappeared, but she complained of the local pain over the canine area. There was complaint of occipital headache also. The remaining 4 teeth on that side were extracted in two sittings, and a course of vitamin B and general tonic were suggested. The gums were treated in the routine method. The patient recovered completely. For about 2 years now she has been perfectly well.

Tic douloureux

It is another painful malady which is very difficult to tackle successfully. It is a persistent spasmodic neuralgia of the trigeminal nerve, accompanied by excruciating pain and contraction of the facial muscles. The aetiology is unknown. It may be caused by any chronic irritation of the fifth nerve. It is occasionally associated with herpes or herpes zoster in the distribution of the nerve affected. There appears to be ample evidence of disease in the teeth being the primary cause of this disturbance, but unfortunately in my experience complete recovery after the extraction of the teeth has been rare.

The early symptoms of this type of neuralgia is tenderness of the scalp and tissues surrounding the nerve as it passes upwards in its course. Pressure over the supra-orbital notch or foramen usually gives a quick response, even brushing or combing the hair over the tender areas of the scalp may cause pain. There may be pain within the eyeball, often the pain is induced by washing the forehead or by pressure of the hat. The pain is often referred to the teeth, but unfortunately the extraction does not give any permanent relief, though the patient may demand their extraction. A very small number of cases I have found recover spontaneously, but the majority of the cases require surgery sooner or later. Alcohol injections I have found give periods of relief ranging from 6 months to 2 years, averaging 8 to 10 months.

General nervous disorders

These include mental depression, insomnia, dizziness, insanity, etc. During my practice I have found that mental disturbances are very often due to infected and impacted teeth. Favourable results may be expected by removal of oral sepsis in case of slight mental derangements. With more serious types however the removal of oral sepsis has not brought about recovery.

Case history.—Mr. S. G., aged 36, artist, apparently of very sound health, gradually developed insomnia ultimately resulting in severe mental depression and melancholia verging to partial insanity. This continued

for one and a half years, by which time the patient was reduced very much. He used to weep most of the time. Treatment for insanity was given without any appreciable effect. The patient was a government servant so he had to appear before a medical board for invalid pension, but a member of the board, an eye-surgeon, finding the condition of his teeth and gums very bad suggested complete dental treatment. The patient was referred to me when the following conditions were noted :—

Teeth.—Lower left third molar badly decayed and not in good position. Lower right third molar impacted and the x-ray examination showed it badly pressing against the second molar, but the patient had no complaint.

Gums.—Spongy, bled easily and in upper right 1 and 2, and upper left 1 and 2 badly pyorrhetic with receding gums.

Lymphatic glands were not enlarged, thyroid normal in size, both lobes symmetrical.

Smears from gums showed numerous pus cells, many epithelial cells, considerable mucus, Vincent's spirilla and fusiform bacilli.

Blood picture.—R.B.C. 4,110,000; W.B.C. 11,800; hæmoglobin 78.

Urine.—Acid reaction; specific gravity 1.009; no sugar or albumin, a few cells of squamous and round epithelium.

The clinical examination and laboratory data indicated Vincent's infection of teeth.

Following recommendations were made :—

1. Increase in caloric and vitamin content of his dietary.
2. Increase in consumption of water to 8 to 10 tumblers (for 2 to 3 he used to consume).
3. A tonic in the form of nux vomica x before meal.

One and a half months later another culture from the gum was done and the following was the additional report :—

Upper gums.—Practically a pure culture of *Streptococcus viridans* with a few colonies of *Staphylococcus albus*.

Lower gums.—*Streptococcus viridans* in pure culture.

Final diagnosis was streptococcal stomatitis.

Routine treatment for the above disease was given for 3 weeks, then the impacted tooth was extracted under nitrous oxide gas, so also the upper 4 teeth and the decayed lower left third molar (2 teeth at a time). During the course of the treatment the patient was improving and after the completion of the whole dental treatment was practically normal. Four weeks after this the patient became absolutely normal and joined the service again.

Oral sepsis is one of the most prevalent sources of nervous disorders although it does not always produce disturbances of this nature until the resistance of the patient is lowered by age, malnutrition, pregnancy, influenza, exposure, grief, worry or fear.

ERRATA

PENICILLIN THERAPY COMPARED WITH SULPHONAMIDE THERAPY IN CEREBRO-SPINAL FEVER

By S. G. VENGSAKAR, V. C. MANKODI and D. D. VAIDYA
(I.M.G., 81, 1946)

On page 113, column 2, line 39, substitute 'for' by 'in'.

On page 114, column 1, lines 46-47, substitute 'sodium sulfadiazine 50 c.c. of 25 per cent strength' by 'solution of 2.5 gm. of sodium sulfadiazine diluted to 50 c.c. with distilled water or glucose solution (50 c.c. of 25 per cent strength)'.

On page 114, column 1, lines 58-59, after '2.5 gm. after 24 hours' add 'and repeated as required thereafter'.

On page 115, column 2, lines 25-26, substitute 'in the group' by 'in the penicillin group'.

TREATMENT OF ORIENTAL SORE BY X-RAYS

By G. PANJA
(I.M.G., 81, 1946)

On page 251, column 2, line 20, for 'an inch' read 'a millimetre'.

A Mirror of Hospital Practice

A CASE OF NEUROMYELITIS OPTICA

By M. N. DE, M.B., M.R.C.P. (Lond.), F.S.M.F., F.N.I.
Professor of Medicine and First Physician, Medical College Hospitals, Calcutta

and
JYOTSNA RANJAN CHATTERJEE, M.B.
Research Assistant under the Professor of Medicine, Medical College Hospitals, Calcutta

A YOUNG, married Hindu lady, 22 years old, came to the out-patients department of the Eye Hospital, Medical College, Calcutta, on 27th February, 1946, with the following complaints : Since 20th February, 1946, she noticed dimness of vision in the right eye which rapidly became completely blind. Two days later, the left eye was affected which also became blind within two days. On enquiry she said that she had been suffering from slight intermittent fever with frontal headache since 18th February, 1946.

Past history.—Malaria one year ago, kala-azar 6 months ago for which she took one course of antimony injections. No history of syphilis. Married seven years. Two healthy children,

the last child being two years old. No history of abortion.

Subsequent course.—She complained of a dull ache in the lumbar region and felt difficulty in emptying the bladder. For this reason she was admitted into the hospital. On the day of admission she complained of extreme weakness of the right lower extremity and moderate weakness in the left.

Examination of the eyes revealed the following : No perception of light. Pupils widely dilated and not reacting to light. Papillitis both eyes but more extensive in the right. Other cranial nerves normal. Motor power : complete loss of power in the right lower limb and paresis in the left. Power in the upper limbs normal. The muscles of both lower limbs hypotonic. No atrophy, fibrillation or tremors.

Reflexes.—Knee and ankle jerks absent on the right side but present on the left side. Biceps, triceps and supinator jerks normal on both sides. Babinski's sign positive on both sides and superficial abdominal reflexes absent on either side.

Sphincters.—Involved, there being retention with overflow incontinence. Constipation, very marked.

Sensations.—Not impaired.

Her blood pressure was 98/70 mm. of Hg. She had slight fever. She was transferred to the ward of the senior writer on 2nd March, 1946. On examination it was found that in addition to the loss of power in her lower limbs her lower intercostal muscles, specially of the right side, were also affected causing some respiratory distress. Knee jerks were lost on both sides, ankle jerks were absent on the right side but diminished on the left side. Tendon jerks in the upper limbs were normal. Babinski's sign was positive on both sides. Superficial abdominal reflexes were lost on both sides, skin sensations were impaired in the right lower limb and right half of the abdomen extending up to the level of 8th thoracic segment. Joint sense and co-ordination were normal.

She had to be catheterized regularly and constipation was relieved by enema. Spleen was just palpable. Temperature 99°F., P/P 90/22 per minute.

Blood examination :—

W.B.C.	..	8,750 per c.mm.
Polymorphonuclears	..	62 per cent
Lymphocytes	..	26 "
Monocytes	..	2 "
Eosinophils	..	10 "
Blood urea	..	44 mg. per cent
Non-protein nitrogen	..	40 "
W.R.	..	Doubtful

Urine examination :—

Albumen present.
Fair number of pus cells.

Lumbar puncture on 5th March, 1946 :—

Clear.
Tension normal.
Total protein 55 mg. per cent.
No increase of cells.
Langes' colloidal reaction paretic type (5555321000).
W.R.—Doubtful.

Subsequent progress of the case.—From 14th March, 1946, her condition began to improve. The motor power of the left lower limb recovered first and then that of the right. The sensation returned earlier in the right lower limb. On 26th March, 1946, she could count fingers; power in the right lower limb returned. Her knee and ankle jerks became exaggerated on both sides. Babinski positive on both sides. During the convalescence period she developed a *B. coli* infection of the urinary tract which however was promptly controlled by hexamine. A slight bed sore developed in the buttocks but healed up very quickly. On 18th April, 1946, she could walk without support and see things of different colours. Fundus showed optic atrophy following optic neuritis on both sides. The patient was discharged on 30th April, 1946, at her request with marked improvement in her nervous system and complete recovery of sphincter control. She however complained of haziness of vision.

In the hospital she was put on heavy doses of vitamin B₁ injection and an iodide mixture.

Although transverse myelitis leading to paralysis of both the lower extremities is fairly common, the simultaneous involvement of the spinal cord and the optic nerves is met with occasionally only. Such a clinical condition develops in an acute demyelinating disease called neuromyelitis optica which is very much akin to disseminated sclerosis in its pathological process but differing from the latter clinically by simultaneous involvement of both the eyes leading to complete and permanent blindness and also the spinal cord followed by complete paraplegia. In the majority of cases the disease is fatal. The blindness is due to the development of bilateral retrobulbar neuritis which may precede the myelitis by a variable period or vice versa. The paraplegia is due to the development of an inflammatory plaque producing demyelination of the fibres of the spinal cord.

The writers offer their thanks to Captain E. J. Somerset, I.M.S., Professor of Ophthalmology, Medical College, Calcutta, and also to the Superintendent, Medical College Hospitals, Calcutta.

AN ATYPICAL CASE OF MEASLES

By B. B. RAI, M.B., B.S.

Divisional Surgeon, St. John Ambulance, Bareilly

I was called in to see a case of a healthy young boy of ten, on the evening of 10th May, 1946, who suddenly started diarrhoea.

There was no particular history except that he had passed a few loose motions. Of course, he complained much of griping. He was on ordinary indigenous drugs and was given *khichri* in diet. The stools contained much of faecal matter. The temperature of the patient was 100°F. Next morning the frequency of the motion increased, and stools contained blood-tinged mucus. Griping was very agonizing. The temperature shot up to 103°F. and came down to 99°F, next morning. This trend of temperature continued up to the seventh day. He was put on kaolin and bismuth with castor oil. Next day he was put on sulphaguanidine. He did not show any appreciable improvement. On the other hand restlessness and griping increased. The tongue was heavily coated, and was bright red in colour at the edges. Later on, it was suspected to be a case of typhoid fever, diarrhoea being a complication. Tenesmus and frequency of motions (blood-tinged mucus) did not diminish. In view of severe tenesmus, temperature 103°F. and blood-tinged stools consisting of mucus mostly, I suspected the possibility of infective colitis and put him on cibazol with glucose. After two days there was some relief in tenesmus and stools. On the eighth day to my surprise his face disclosed a rash similar to sulphonamide rash. Next day, there was cough, eyes were congested and watery and the rash appeared on the whole body and it was a frank case of measles. On the fourth day the temperature went down, motions and tenesmus stopped. The patient was fed on orange juice and no medicine was given after the appearance of rash.

Therapeutic Notes

NOTES ON SOME REMEDIES

I. MEPACRINE IN MALARIA

By R. N. CHAUDHURI, M.B., M.R.C.P. (Edin.),
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It is now fifteen years since atabrin was first introduced by the Germans as a synthetic substitute for quinine, the supply of which was lost to them during the 1914-18 war. But, while the German inventors published the formula of the drug, they did not reveal some of the essential features of its manufacture, and it had to be imported or imitated. Attempts at imitation by different firms were eventually successful, but gave rise to a variety of names for what is considered to be the identical drug, the British product being known as mepacrine, the American quinacrine, and the Russian aciquine. It played a very important part during the war years in both civilian and military practice, and it may be said that the Allies owed their escape from a dangerous position to the enterprise of the German chemical industry, though British and American scientists soon rose to the occasion and were able to produce the needed drug. As mepacrine may continue to be our chief drug in malaria for sometime to come, a brief description of its uses embodying our recent knowledge may be of some use to the practitioners.

Mepacrine is an acridine derivative, and its dosage and period of administration were calculated so as to obtain a therapeutic effect more or less equivalent to that of quinine without toxic reactions. This dosage was (and is still often followed in civilian practice) 0.1 gramme three times a day for five days for a clinical cure and 0.2 gramme twice a week for clinical prophylaxis or 'suppression'. After oral administration, mepacrine is rapidly absorbed from the alimentary canal and a large percentage is fixed in the tissues. The rate of excretion is slow, and therefore traces are found in the urine for weeks after the drug is discontinued. As it circulates in the blood, it is absorbed by the red cells and acts directly on the malaria parasites. This is in contrast to the action of quinine, which even in big doses, produces little morphological changes in the parasite. In vivax malaria, mepacrine like quinine has an effect on all the developmental stages of the parasite in the peripheral blood, although the gametocytes are the last to disappear. In falciparum malaria it is definitely superior to quinine so far as the ring forms are concerned, but it is ineffective on the crescents. The immediate effect of mepacrine in an acute attack is undoubted; the fever, as a rule, falls after the first three days of its administration.

In 1942, after the loss of Java and its quinine supplies, mepacrine became the mainstay of the Allied forces operating in malarious areas. Special research work on its pharmacology was started, and its properties were studied intensely. Particular attention was given to the estimation of the drug in the blood and to the guidance to be obtained therefrom. It was found that when repeated small doses are given over a period of days or weeks, there is progressive accumulation of the drug in the body, especially in the liver, and along with this there is an increase in the plasma mepacrine concentration; eventually a fairly uniform level in the plasma is achieved, and no further significant changes in the mepacrine content are observed, even after prolonged administration of the drug and in spite of the fact that it is excreted slowly through the urine and faeces. This is due to its extensive localization in various organs and it is also probable that some of it is destroyed or chemically changed in the body. Once it is discontinued it is slowly but almost completely eliminated from the body, leaving no detectable damage to the liver or other tissues, and no apparent effect on the general health. It has been shown that the anti-malarial activity of mepacrine is related to its concentration in the plasma. The concentration necessary to effect a clinical cure in malaria varies with the individual and also with the strain of parasite, but a certain minimum level is required (about 30 microgrammes per litre). It was found that on the ordinary therapeutic doses already mentioned, an adequate plasma level was often not attained. The necessity of increasing its dosage thus became obvious. It was pointed out that there was need of large initial 'loading' doses, as in the case of sulphonamide therapy, to raise the blood concentration to the desired level and for appropriately spaced maintenance doses. So it became the army practice, at least in highly malarious places, to use bigger doses, e.g. 0.2 gramme immediately and every six hours during the first 24 hours, a total of 1.0 gramme and then 0.1 gramme thrice daily for 6 days, i.e. 2.8 grammes in all. These trials were mostly made on the American and British troops who are heavy, well nourished and non-immune, having no previous attack of malaria. For our civilian use among people of smaller weight, often with some degree of malarial immunity, some modification of the dosage is necessary, hence a simplified method has been started empirically by giving 2 tablets twice daily for 4 days, keeping the total dose, 1.6 grammes, i.e. almost the same as originally suggested.

With regard to its use by injection, the German preparation was found to be toxic. The British and American preparations are said to be safer and are used by the army for severe cases of malaria when the patient is having too much vomiting, is unconscious, or has a particularly heavy *P. falciparum* infection.

We have little or no experience of it and usually use quinine for such cases, but there is a tendency now to substitute intramuscular mepacrine for intravenous quinine in pernicious forms of malaria. For parenteral use a dosage of 0.2 gramme is given every six or eight hours but returning to the oral route as early as possible. Although injections of mepacrine effectively control an acute attack, their routine administration is not advisable as they have been known to cause nervous disturbances.

As regards the prophylactic value of mepacrine, opinions were at first divided. Some thought it was not only ineffective, but gave greater relapse rates, while others thought it was superior to quinine. Even amongst the latter there was no general agreement on the dosage and the method of administration. It may not therefore be uninteresting to know the results of the army's experience in this matter in the last war. In areas where the malaria risk was slight, it was found that a total weekly dosage of 0.4 gramme acted as an efficient suppressive, but in highly malarious areas the dose was 0.6 to 0.7 gramme, i.e. one tablet a day. It has been shown that sufficient plasma mepacrine concentration (12 microgrammes) is obtained with this dosage given for two weeks prior to entry into an endemic area, but this period may be shortened by doubling the dose for the first week, or by a 'loading' dose of 0.6 gramme on the first day, and continuing with the daily dose of 0.1 gramme. This therapy does not prevent malarial infection, but has a most valuable action in suppressing the clinical manifestations. This is shown in a reduced number of clinical attacks and a lesser severity of such attacks as are not prevented. If the suppressive treatment is continued for two weeks after the risk of infection has disappeared, M.T. infections are sterilized, but not the B.T. infections many of which are only rendered latent and may flare up within a few weeks after treatment ceases or reveal themselves even after 6 to 9 months.

Much has been said about the toxic effects of mepacrine. There is however good deal of misunderstanding on the subject. In ordinary therapeutic doses that we use, mepacrine is not toxic, but occasionally intolerant symptoms are seen. These are : (1) gastro-intestinal disturbances such as abdominal pain, vomiting and diarrhoea, and (2) nervous and mental symptoms. There may be abrupt change of behaviour with motor and psychomotor activity, or there may be fits of depression, delirium, convulsion or psychosis. These symptoms usually begin just before or after the completion of the treatment. There is no objective neurological disturbance. Considering its widespread use, these effects may be said to be uncommon, and when they do occur they are usually temporary. They have occurred more frequently when the treatment was unduly pro-

longed and when the doses were excessive, especially when given simultaneously with mepacrine injections or with pamaquin. It must also be remembered that the untoward symptoms may be due to the disease itself. In the army the drug has been given in prophylactic dosage daily over periods of a year or over without demonstrable ill-effects apart from an incident in 1943 when about a third of the men taking mepacrine (0.2 gramme twice weekly) were stricken with vomiting, cramps and diarrhoea after the third dose had been taken. Why this happened is still a mystery. However, while taking the first few doses, some may complain of slight unpleasant side-effects mainly gastrointestinal, but they soon disappear if the treatment is persisted in. These effects can be prevented in most cases by giving sodium bicarbonate or sweetened drinks along with the drug. The more serious nervous complications are more rare, but invariably clear up sooner or later, with the discontinuance of the drug and administration of sedatives. The frequent discoloration of the skin which alarms some patients is, of course, due to deposit of the dye in the tissues and not the effect of any toxic action. This does not harm the patient and gradually clears up after cessation of the treatment. It may be too early to pronounce on the remote effects after prolonged administration of mepacrine. Longer observations are needed to find out whether the thousands of men in the army develop any pathological state as a result of large doses of mepacrine given therapeutically as well as prophylactically during their service. But whatever the ultimate result may be, there is no doubt that, during the last war, it played a vital part in reducing malaria and saving thousands of lives. The toxic side-effects are few and should not be over-emphasized. In a series of 7,604 cases of malaria treated with mepacrine, 25 developed toxic psychosis, i.e. only 0.4 per cent. At present we have no other drug at our disposal that does what mepacrine cannot do, namely destroy the sporozoites injected by the mosquito, and prevent relapses in benign tertian malaria.

Thus mepacrine is an efficient synthetic substitute for quinine. It is cheap and easily available. It is easily taken by mouth and readily absorbed but slowly excreted which is an advantage in therapy and certainly in suppression of malaria. It is safe in blackwater fever; it is safe in pregnancy; it is safer than sulphonamides and very much safer than to have M.T. malaria untreated, so that no apprehension of toxic psychosis which is rare should prevent its use. In individual drug prophylaxis mepacrine is the drug of choice and can be safely recommended to anyone visiting a malarious country. But research for new synthetic anti-malarial drugs is going on, and a recent one, paludrine, has shown promising results. It is still in the experimental stage, and we shall deal with it in our next article in this series.

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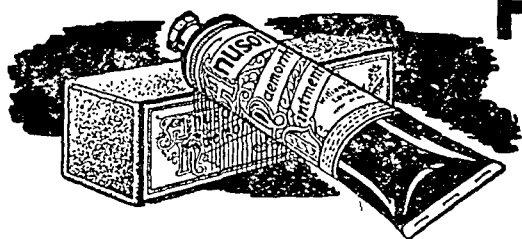
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Indian Medical Gazette

SEPTEMBER

VENEREAL DISEASES OTHER THAN SYPHILIS, GONORRHOEA AND SOFT SORE

THERE are two such diseases and they appear to be confused by the venereologists themselves, in the matter of nomenclature at least. They are :—

1. *Lymphogranuloma Inguinale*.—It is also called (i) lymphogranuloma venereum (Tobias, 1945) and even, quite wrongly, (ii) granuloma venereum. Here is an abstract from

tropical bubo (Lomholt, 1945). Lymphogranuloma inguinale is preferable to all other names.

2. *Granuloma Venereum*.—Its recognized synonyms are (i) granuloma inguinale (Wilson and Miles, *loc. cit.*), (ii) granuloma venereum inguinale (Lomholt, *loc. cit.*), (iii) granuloma, ulcerative, (iv) ulcerating granuloma of the genito-inguinal regions, (v) tropical granuloma, (vi) chronic venereal sores, (vii) serpiginous ulceration of the groin (Rajam, 1937). Granuloma venereum is preferable to the other names.

In the matter of diagnosis the situation is further confused by the occurrence in the groin of buboes consequent on a chancre.

The following table (after Tobias, *loc. cit.*; modified) summarizes the venereal lesions, other than those of syphilis and gonorrhoea, in the groin.

TABLE

Differential diagnosis of venereal lesions, other than those of syphilis and gonorrhoea, in the groin

	Chancroid	Lymphogranuloma inguinale	Granuloma venereum
Bacteriology ..	<i>Haemophilus ducreyi</i>	Virus	<i>Donovania granulomatis</i> *.
Systemic disturbances ..	None	Yes	None.
Frei test ..	Negative†	Positive	Negative.
Ulceration ..	Without induration	Suppuration	Deep and extensive with vegetations and granulomas.
Adenitis ..	Present in 30 per cent of cases.	Characteristic. Low grade inflammation of the lymph spaces, lymph channels, and nodes leading to caseation, formation of fistulas, fibrosis and esthiomene.	None as a rule. In rare cases, however, inguinal adenitis or bubonuli may be seen. Esthiomene may also occur.‡
Pain	Yes	No	No.
Incubation period ..	About three days	Ten days to three weeks	Long.

* A specific human bacterial parasite, resembling bacilli of the Friedlander group and having unique growth requirements (Wilson and Miles, *loc. cit.*).

† Some cases may react to the Frei test for lymphogranuloma inguinale. There is a reciprocity between the chancroid and the lymphogranuloma inguinale some cases of which may react to the Ducey antigen (Wilson and Miles, *loc. cit.*). The test with this antigen is not included in the table. Both tests, specially the one with Frei's antigen, remain positive long after recovery.

‡ Andrews, 1946.

'Experimental transmission of lymphogranuloma venereum virus through the placenta' (*Amer. J. Surgery*, December 1945, vol. 70, no. 3, 320-38, 18 figs., 22 refs.): 'Lymphogranuloma inguinale virus was injected into pregnant mice. The offspring were proved to be infected with the virus as judged by the occurrence of clinical signs, the presence of elementary bodies, and the fact that Frei antigen made from foetal brain proved positive in human cases of the disease' (Rhodes, 1946). The disease under description in the article abstracted was lymphogranuloma venereum which became lymphogranuloma inguinale in abstraction. Recognized synonyms of lymphogranuloma inguinale are (i) climatic bubo, (ii) lymphopathia venereum, (iii) poradenitis (Wilson and Miles, 1946), and (iv)

Two additional conditions, *ulcus vulvae acutum* and *ulcus insons puellarum*, described by continental observers (Lomholt, *loc. cit.*), are probably identical and probably non-venereal. They are rare, non-characteristic and seen only in females, mostly in children. *Bacillus crassus* has been demonstrated in some cases to be the cause. The lesions appear as small, superficial, crust-covered ulcers with sharp edges, usually on the labia. Occasionally fever and swelling of the inguinal glands are present. Prognosis is good. Need for differentiation from diseases which are definitely venereal is obvious.

The lesion commonly known as venereal warts should preferably be called *verruca acuminata*, as gonorrhoea is only one of the several predisposing causes: the exciting cause is probably a virus

(Tobias, *loc. cit.*, Wilson and Miles, *loc. cit.*). Unfortunately the lesion is also known as condyloma acuminatum.

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THREE IMPORTANT MEDICAL ANNOUNCEMENTS

In this issue of the journal, under 'Current Topics', will be found announcements in America concerning three important items: (1) Streptomycin. The makers have appointed a committee to recommend supplies to recognized institutions in America. (2) Treatment of syphilis with penicillin. Records more complete than have been available so far are presented. (3) Treatment of neuro-syphilis with penicillin. Encouraging results have been obtained.

Medical News

MASS-PRODUCED STANDARD HOUSES FOR WORKERS: BULK ORDERS TO LOWER COSTS HOUSING COMMITTEE'S REPORT

CO-ORDINATION of building programmes through a National Industrial Housing Board, and lowering of costs by mass production of standardized parts and bulk-buying of material are recommended in the Report of the Industrial Housing Sub-Committee, which is to be considered by the Standing Labour Committee at its next meeting in July.

The committee feel that there is urgent need for research into improved methods of building construction and recommend that the Central Government should take immediate steps to set up a technical committee to examine the question of reducing the present high cost of construction and the rationalization of the brick industry.

Dealing with mass production and its effect on construction costs the committee say: 'Bulk orders, if possible, at controlled rates, should be placed by the Board for these materials through the Industries and ...'

Our housing programme is so large and will be spread over so long a period that, if properly planned and co-ordinated, the very size of the orders should enable a very large reduction in prices to be obtained. We recognize that houses in different parts of India must, owing to climatic conditions, differ in their details. Nevertheless, there will be very large quantities of fittings and parts of a standard house which could be mass produced at big reductions on the prices ruling for piecemeal manufacture.

They emphasize the importance of controlling the location of factories by a system of licensing which would include approval of the factory site as one of the conditions of any permit, in the solution of the housing problem. This would avoid congestion in the already overcrowded main cities.

Provinces and local bodies, the committee recommend, should be requested to report within a short specified period the existing shortage of industrial housing in their areas.

Building fund

The committee consider that there should be a building fund for financing the housing of workers who are unable to pay an economic rent. The fund could be raised by either the Central Government or the Provincial Government or both making available long-term, interest-free loans for housing built to approved standards. Such loans should be redeemed by the building authority by means of a sinking fund spread over a period of not less than 30 years.

The housing fund and the housing subsidy should be administered by a National Industrial Housing Board, consisting of representatives of the Provinces, the Central Government, the States, employers, workers and other interested parties. In addition to this board, regional boards representing Provincial Governments, States, local authorities, employers and workers should be set up to co-ordinate regional schemes. To enable a start to be made, the committee recommend that Provincial and Central Governments between them provide the necessary finances in the form of long term, interest-free loans for private schemes. In addition to this, they suggest that employers should be asked to pay a sum of Rs. 2 per house per month for every house allotted to them. Any deficit remaining over and above that covered by employers' contribution and the loan should be met by a further subsidy raised by general taxation.

Properly developed sites for housing schemes should be made available by the provincial and local authorities. In the opinion of the committee, local authorities should be responsible for the provision of all public amenities.

Minimum standards

The standards recommended by the sub-committee envisage a lay-out on the lines of a garden city, with not more than 20 single-story houses to an acre except in certain congested areas like Calcutta. The minimum standard of accommodation should be two rooms for every family, with an area of 240 sq. ft. and no room with a cubic capacity of less than 1,000 c.ft. Each house should have at least one verandah, a courtyard, a kitchen with chimney or flue, a family lavatory and covered drains. They should be well ventilated and preferably electrically lighted. Public amenities like playgrounds, schools, hospitals and shops should be provided. Provision of adequate and cheap transport facilities for the workers is considered a part of every housing scheme.

As regards the basis on which rent should be recovered from workers, the committee were unable to arrive at any agreed decision. The workers' views were that rent should be charged on a sliding scale ranging from 2 per cent of the wages in the case of labourers earning below Rs. 20 per month to 10 per cent of the wages in the case of those earning more than Rs. 50 a month. Others were of the opinion that houses should be classified into three grades and rent charged according to each grade on the basis of Rs. 2 per

100 sq. ft. of room space. On this basis the rent of a minimum-standard house would be about Rs. 5 per month. The majority of workers in cities like Bombay and Calcutta are paying more than this for a room in a chawl or bungalow.

The Industrial Housing Sub-Committee were appointed by the Standing Labour Committee in its seventh session held on 28th August, 1945, with Mr. Gordon Peace, Chief Adviser, Factories, as chairman, Sir Shri Ram, Sir Edward Souter and Messrs. V. V. Giri, P. T. Borale, J. N. Mitra, W. H. Prosser, B. R. Kagal, K. S. Srikantan, B. G. Appadorai Mudaliar, N. A. Mehrban and H. I. Matthews as members. Mr. N. S. Mankiker was secretary.

ROYAL COLLEGE OF SURGEONS OF ENGLAND: PRIMARY EXAMINATION FOR THE F.R.C.S.

1. The Primary Examination in Anatomy (including normal histology) and Applied Physiology and the Principles of Pathology will be conducted at Madras.

2. The examination will begin with the written paper on Monday, 23rd December, 1946.

3. Each candidate will be notified in writing of the result at the termination of the examination.

4. The examination is open to the following candidates (men or women), viz.:-

(a) Those possessing a qualification which is registrable in the British Medical Register; and

(b) those possessing the degrees in medicine and surgery of a university recognized by the Council of the Royal College of Surgeons of England for the purpose.

Note 1.—The degrees of the following universities in India are recognized for the primary examination: Andhra, Bombay, Calcutta, Lucknow, Madras, Patna, Punjab, Rangoon, Mysore and Osmania.

Note 2.—Unless a candidate's name appears in the British Medical Register a certificate from his university giving the date and description of his medical and surgical degrees must accompany the Form of Application.

5. Copies of the regulations, and of the Form of Application for admission to the examination, may be obtained, free of charge, from the Director of Examinations, Royal College of Surgeons of England, Examination Hall, Queen Square, London, W.C.1.

6. The fee for admission, or readmission, to the examination is £35 sterling, which must be sent with the Form of Application, so as to reach the Director of Examinations at his office (see clause 5 above) not later than Saturday, 28th September, 1946.

7. Candidates who withdraw from the examination (owing to illness or any other cause) after their entries have been accepted will be refunded half the amount of the fee paid for admission to the examination.

8. With the exceptions noted above, the examination will be conducted in accordance with the published regulations for the Fellowship of the Royal College of Surgeons of England.

HORACE H. REW,
*Director of Examinations,
Royal College of Surgeons of
England.*

FEDERAL SECURITY AGENCY, U.S. PUBLIC HEALTH SERVICE, WASHINGTON 25, D.C.

The Surgeon-General, U.S. Public Health Service, Federal Security Agency, has published a report regarding the release of officers on active duty with the Public Health Service. Detailed information may be obtained from his office.

APPALLING CONDITIONS IN INDIA'S DAIRY INDUSTRY

The following is copied from the *Journal of the American Medical Association*, Vol. 130, No. 4, 6th April, 1946, p. 963:—

'A report to the Government of India by Mr. R. A. Pepperall, chief executive officer of the British Milk

Marketing Board, reveals appalling conditions in India's dairy industry. The efficiency of the industry is considered by the author to be the lowest in the world. Adulteration by adding water to milk was usual at all stages of distribution from producer to consumer. In Calcutta the added water exceeded 25 per cent. The conditions of milk production in Indian stables are described as "starvation of stock, squalor, filth, ignorance or indifference toward hygienic principles, and revolting personal habits, allied to official apathy". At one Bombay stable housing hundreds of animals, in which conditions might be regarded as normal, the author observed crows feeding from a dead buffalo and then drinking from milk containers. At another stable the buffaloes were allowed to immerse themselves daily in a backwater in which were deposited the urine of 500 animals and in which there were dead animals. Udders were not washed before milking. Official reports showed a bacteria count of 36 million per cubic centimetre for Bombay milk. Although milk production in India is declining, the population is increasing. The price of milk is the highest in the world. The author points out the unparalleled dimensions of the problem of reorganizing an industry consisting of 22 million illiterate and poverty-stricken producers with semi-starved livestock.'

NINTH CLINICAL MEETING OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE, HELD ON WEDNESDAY, 5TH JUNE, 1946

MAJOR ANDREASEN showed two cases of tumour of the superior maxilla with the object of emphasizing the relative commonness of the condition in Bengal, and further illustrating how they differ in radio-sensitivity. Each had had a palate application of 12 mg. radium for 7 days and 5 days with 5 days' interval. The larger tumour showing calcification in the radiogram remained unaffected; the second one showing osteolysis melted before the radium application. Plaster casts of the cases before radium were shown with the cases to prove the changes. Major Andreassen explained that these tumours may arise from the antrum but more often from the ethmoids or the surface of the maxilla in the region of the alveolus. Richard Wiseman, Sergeant Surgeon to King Charles II, gives the first account of surgical attack on one of these tumours. He, in 1671, operated, with cautery and digestives, upon a young man of 28 whom he judged to be suffering from a sarcoma. Ambrose Pare recognized malignant tumour of the upper jaw, but Percival Pott distinguished between benign and malignant quite clearly. Robert Liston, trained in Edinburgh and famed in London, considered his own success in operating upon these tumours due to the technique taught him by Prof. Lizars of Edinburgh. This is the first account of formal removal of the upper jaw. Sir Henry Butlin and Douglas Harmer of Barts did much in the early part of this century to bring operative treatment into favour. More recently with the advent of deep x-ray treatment, these tumours like many others have been relegated to deep radiation without much clinical attention. That all do not respond to radiation is illustrated by the two cases shown; that where deep x-ray is not available a reduction in the palatal part of this tumour may be effected and so render any ultimate operation technically easier is shown by the response of the second case.

Dr. A. K. Sen discussed the importance of argemone oil as an adulterant of mustard oil and described the nitric acid, the cupric acetate and the ferric chloride tests as used for the detection of the oil. He further pointed out that the ferric chloride test as carried out by him was easy to perform, sensitive, detecting speedily 0.25 per cent of argemone oil and is specific because it produced characteristic needle shaped crystals. The crystals isolated by him were demonstrated under the microscope, by microphotographs and by other methods.

Dr. G. Panja discussed a case of multiple benign hamangioma similar in structure to sarcoids in epidemic

dropsy. The patient, a Hindu female, aged about 25, of fairly good health, started getting, about 8 months ago, small reddish rounded elevations on the skin in various parts of her body, most marked on the buttocks and the extremities. The tumours began to increase in size and some attained the size of a small plum and became pedunculated. Fresh tumours appeared now and then, and there were 14, one on the chin, two on the neck, two on the back and the rest on the extremities. On diascopy of the small tumours, the red colour in smaller ones disappeared giving place to brownish stippling. The tumours were solid to feel and painless and due to friction with clothes some got excoriated on the surface. There was bleeding from the excoriated surface when roughly handled. Enlargement of glands absent; heart, lungs, liver, spleen, etc., showed no abnormality; a septic mouth associated with extensive pyorrhœa alveolaris present. There was no history of epidemic dropsy, neither in herself nor in the family. There was an attack of malignant tertian malaria two years ago. Culture from an excoriated tumour showed *Staphylococcus aureus* and *Ps. pyocyanea*. The tumour was not a typical sarcoid of epidemic dropsy as there was no history of the disease, the tumour did not bleed very much on trivial injury and did not fill up gradually after release of pressure, and on histological examination the capillary vessels were not found engorged with blood. It was also not (i) a multiple benign sarcoid (lupoid) of Boeck where there are circumscribed masses of epithelioid cells and face is the site of predilection, (ii) a Spiegler Fendt type of sarcoid where round cells preponderate, (iii) a Darier Roussy type of sarcoid as the Mantoux test was negative and its tuberculous nature had not been demonstrated by animal inoculation and finding of *Myc. tuberculosis* as reported by Philipson in the Darier Roussy type, (iv) an ordinary capillary hæmangioma which is usually congenital, (v) telangiectasis as it was not characterized by dilatation of previously existing blood vessels, and was larger in size, and (vi) a granuloma pyogenicum as history of pyogenic local infection and of typical granulation tissue was absent (see photograph, plate XXII).

Dr. P. C. Sen Gupta demonstrated a patient with kala-azar who had developed complete agranulocytosis towards the end of a course of injections of a pentavalent antimony compound. The onset of agranulocytosis was associated with the occurrence of high fever. There was no evidence of serious septic complications during the height of fever and the fever persisted until the appearance of neutrophils (over 250 per c.mm.) in the blood, when it came down by crisis, 5 days after the commencement of treatment for agranulocytosis. The case was successfully treated with penicillin, pentnucleotide, liver extract followed by pentavalent antimonials.

Dr. Lowe showed a patient with vomiting, hepatitis, jaundice, oliguria and hæmaturia, and multiple petechial hæmorrhages, following the bite of an unidentified creature in long grass. The symptoms appeared within one hour of the bite. There was practically no local lesion at the site of the bite. It was considered that the bite must have been that of a viper, possibly a small one, and that a small dose of venom insufficient to cause rapid death must have entered more or less directly into circulation.

Dr. A. K. M. Abdul Wahed showed a case of patent foramen ovale and Dr. Md. Ibrahim a case of interstitial emphysema.

ANIMAL HUSBANDRY IN ASSAM : UP-GRADING FOR INCREASED MILK YIELD

ANIMAL NUTRITION AND DISEASE INVESTIGATION

THE progress of schemes formulated by the Imperial Council of Agricultural Research, other development schemes and agricultural conditions in Assam were amongst the subject discussed by the Animal Husbandry Commissioner with the Government of India during his recent tour of the Province of Assam. The Animal

Husbandry Commissioner visited the veterinary headquarters at Gauhati and the disease investigation laboratory and veterinary hospitals and cattle farms at Shillong and Sylhet.

Up-grading of stock

The cattle breeding policy to be followed in Assam is to up-grade the stock in order to increase the yield of milk. The cattle there are generally small-sized, yielding scanty milk, which does not materially increase with feeding. Large cattle are unsuitable for work on the small segments of Assam's hunded land. The use of Sindhi sires for up-grading would materially increase the milk yield of the cows and would not adversely affect the work bullocks. The use of these sires is likely to be popular where there is a market for fresh milk. European strains of dairy cattle are already established in and around their use is recommended in other situations.

About five hundred cows have been purchased from the military authorities; and although, says the Animal Husbandry Commissioner, they may not be very useful for immediate milk production, their daily output being very small, they would help to make up the shortage which is said to exist and if they are used for breeding with Sindhi or Tharparkar bulls, their progeny should be distinctly superior. It would, however, be cheaper and just as effective if this grading work were entrusted to private cultivators on certain conditions, and not done on Government farms.

The buffaloes at the Sylhet farm could be up-graded with the Murrah type and thus made to yield fairly good supplies of milk. These animals could be fed on aquatic plants supplemented with concentrates.

Poultry farming

Poultry farming is on the increase in Assam, but it should be borne in mind, says the Animal Husbandry Commissioner, that above a certain level poultry population competes with human population for cereals. With bountiful supplies of water and presumably aquatic food, ducks should be cultivated in larger numbers.

Animal nutrition

The solution of the animal food problem in Assam appears to be in the exploitation of the uncultivated grasses and in the encouragement of leguminous crops. Research on these aspects is in operation.

Disease control

In addition to the common Indian contagious animal diseases, bovine pleuro-pneumonia is prevalent and is peculiar to the Province. Control or elimination of contagious diseases would afford a greater measure of relief to the livestock owner than would any other benefit. With this end in view, the development schemes in Assam contemplate a fourfold increase in the number of veterinary surgeons.

TENTH CLINICAL MEETING OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE, HELD ON WEDNESDAY, 3RD JULY, 1946, AT 4-30 P.M.

Dr. L. M. GHOSH showed a case of (?) dermatomyositis. He discussed its clinical aspect and invited suggestions regarding investigation, diagnosis and treatment.

Captain E. J. Harris, R.A.M.C., spoke on melioidosis in Rangoon. Since January 1946, the West African forces have been moved from the north to the south of Burma into a concentration area in and around Rangoon. During the 3 to 4 months ending June 1946, five cases of the disease have occurred amongst these troops. Two of the cases were recognized as such by bacteriological diagnosis at post mortem. The causative organism is *B. whitmori* (otherwise known as *Pfeifferella pseudomallei*, etc.). It is a gram-negative, motile bacillus, existing in fresh smears as a cocco bacillus and frequently exhibiting bipolar staining. It

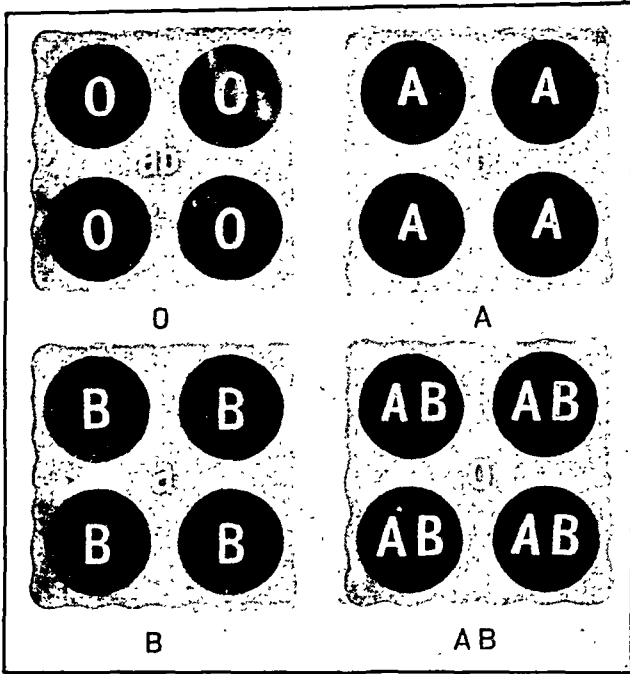


Fig. 1.

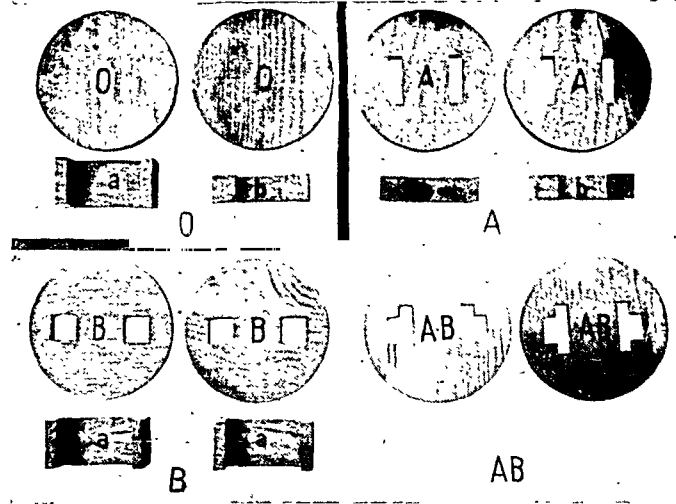


Fig. 2.

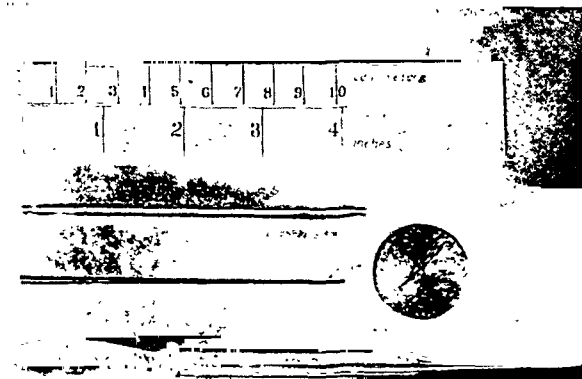


Fig. 3.

1	2	3	4	5	6	7	8	9	10	Centimeters
1	2	3	4							Inches

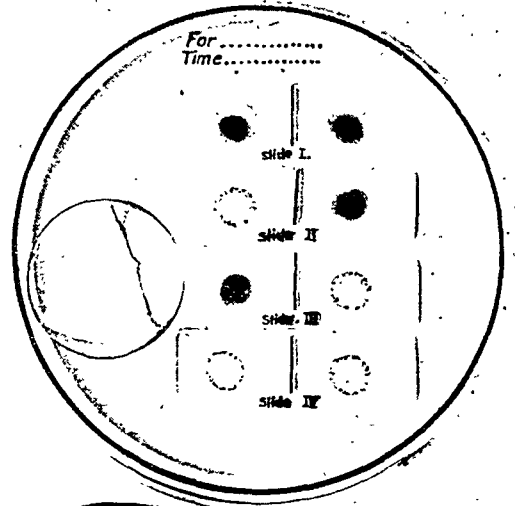


Fig. 4.

PLATE XXII

A SIMPLE METHOD OF ESTIMATING THE TITRE OF KAHN ANTIGEN :
N. SESHADRINATHAN AND B. A. SRINIVASAN. PAGE 357.

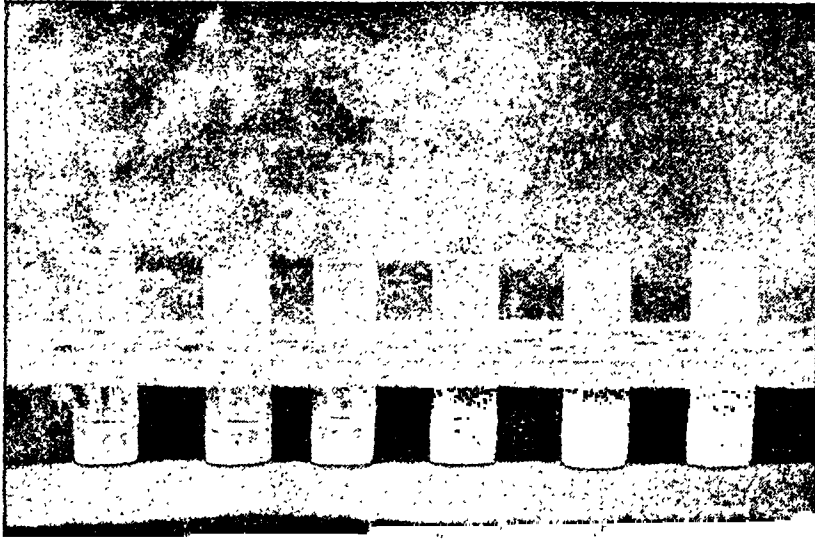


Figure showing the titre.

NINTH CLINICAL MEETING OF THE CALCUTTA SCHOOL OF TROPICAL MEDICINE.
PAGE 367.



Figure showing multiple benign hæmangioma.

grows easily on almost all laboratory media and in 24 to 48 hours the colonies assume a typical button shape. In most instances these have assumed a corrugated surface in another 3 days. Agglutination was obtained in high titre against a specific serum obtained from a rabbit. The ordinary laboratory sugars were fermented with formation of acid but no gas. Captain Harris then described the three cases which were under treatment. The first case had a skin lesion, a few pustules, which had previously been diagnosed as secondary syphilitic, chicken pox and samillpox lesions. On admission the patient showed evidence of a cystitis and urinary culture produced a pure profuse growth of *Pf. whitmori*. The largest pustule on the forehead, which was more like an abscess in reality, was then incised and the pus produced a pure growth of the same organism. In view of the reported synergic action of penicillin and sulphonamide it was decided to give heroic doses of the drugs simultaneously, 2½ million units of penicillin per day and the routine dosage of 1 gramme 4-hourly of sulphathiazole. At the end of five days' course there was no pyrexia and on the 7th to 9th days the urine was sterile. After this the urine showed increasing numbers of organisms and a longer course of therapy was begun and kept up for 7 days. The second case was admitted with symptoms and signs of chest trouble, of no remarkable significance. *Pf. whitmori* was isolated from the sputum and he is making good progress with the therapy adopted in the first case. The third case was a prize case. The patient was admitted and treated as a case of pneumonitis in February and sent to a convalescent home. His x-ray showed a doubtful blurred shadow in the right mid-zone. On readmission for checking progress, x-ray showed some advance in the lesion but no marked physical signs. Some 4 weeks later, in April, x-ray showed cyst formation in the doubtful area and by now this has advanced to a definite abscess with a wall about ½ inch thick. *Pf. whitmori* were isolated from sputum at this time in profusion. Like tuberculosis the appearance of the organism in sputum tends to be spasmodic and probably coincides with a breakdown of an abscess into a bronchus. The abscess cavity was injected with about one million units of penicillin and combined with the massive systemic sulphamezathine, from about 4 inches across it can now be made out only as a ½ inch patch in the x-ray. The disease, however, by virtue of abscess formation does not lend itself very well to this form of therapy. If abscesses are approachable, surgery is advisable to remove as many organisms from the body as possible. *In vitro* experiments cast some doubt on the efficacy of the penicillin, unless the organism can be subjected to local applications of a strength of over 300 units per c.cm. Sulphamezathine in large doses appears to be sufficient for systemic treatment. It is probable that the disease is not as rare as one would imagine and that in well-nourished individuals it is not really as an acute disease as the original literature would indicate.

Dr. John Lowe showed the same case which he showed in the previous meeting and was supposed to be a case of viper bite. The patient was completely cured after a month's stay in the hospital. During this period he developed marked oliguria, almost complete anuria, with anasarca and threatened uræmia. Blood urea was steadily rising to as high a level as 294 mg. per cent. He was treated with isotonic sodium sulphate solution given intravenously about one litre daily for five days. This was followed by a profuse diuresis and gradual decrease in blood urea level to normal. The recovery of the case with sodium sulphate treatment was remarkable.

Dr. R. N. Chaudhuri demonstrated an advanced case of pseudo-hypertrophic muscular dystrophy in a boy aged 12 years. The striking features were 'dropped shoulders', atrophy of the deltoid, pectoralis and the serratus, winged scapula, protruding abdomen, lordosis with slight scoliosis and marked pseudo-hypertrophy of the calves. The boy walked with difficulty, and the gait was waddling. He could not get up from the

supine position although he could do it before in the classical manner. The history was that he was apparently all right up to the age of five years; thereafter a slowly growing disability was noted. Other members of the family were unaffected.

Dr. Chaudhuri also showed a case of pulmonary amœbiasis. The main symptoms were recurrent hæmoptysis and bouts of fever. No clinical or radiological abnormality was detected in the chest. *E. histolytica* was found in the sputum on several occasions and the response to specific therapy was striking each time. In the present attack four injections of emetine had no effect, and it was discontinued as she complained of palpitation. For about a week after admission to the hospital she was given no treatment and she continued to spit blood daily. Then to perform a liver function test she was given an intravenous injection of sodi benzoas which caused a slight febrile reaction but stopped her hæmoptysis.

PENICILLIN IN THE B.P.

(Abstracted from the *Lancet*, i, 1st June, 1946, p. 839)

By an amendment to the British Pharmacopœia, 1932, just issued, penicillinum (abbreviation penicil.) becomes an official medicament. When pure the sodium salt of penicillin is a white powder, in the form of granules or scales, and contains 1,666 units per mg. Sodium or calcium penicillin which is not completely pure is a pale yellow to light brown amorphous powder, containing at least 300 units per mg.; it is hygroscopic, and must therefore be protected from the action of moist air. The salts are very soluble in water, but insoluble in fixed oils and liquid paraffin. The monograph lays down a standard mouse-test for toxicity and a rabbit-test for pyrogens. The salts of penicillin are dispensed in sealed containers and must be stored at a temperature not exceeding 10°C. The label must state which salt is present, the total number of units in the container, and the minimum strength in units per mg.

In appendix xv of the B.P., which deals with biological assay, a new section, lettered X, gives details of the standard preparation of penicillin (a quantity of the dried sodium salt kept at the National Institute for Medical Research), the unit, and the cylinder-plate and broth-dilution methods of estimating potency. There are to be seven official preparations: (1) cream, made with 'Lanette wax SX' or its equivalent and a mixture of paraffins, containing 500 units per ml.; (2) sterilized cream; (3) injection, a sterile solution of the sodium or calcium salt in physiological saline, usual strength 20,000 units per ml.; (4) oily injection, a sterile solution of the calcium salt in white bees wax and arachis oil, dose min. 15-60, which contains 125,000-500,000 units; (5) ointment for the eye, containing 1,000 units per gramme of a mixture of soft paraffin and wool fat; (6) lozenge, weighing 1 g. and containing 500 units; and (7) ointment, containing 500 units per gramme of ointment of wood alcohols.

PENICILLIN IN A NEW VEHICLE

A NEW vehicle for prolonging the action of penicillin consisting of magnesium sulphate monohydrate in peanut oil is described by Donaldson and Allen (*Lancet*, 13th April, 1946). Penicillin has been demonstrated in the sera of 8 out of 11 patients twenty-four hours after a single subcutaneous injection of 250,000 units in the vehicle. Of 617 cases of gonorrhœa, 87 per cent were 'cured' with one injection, and even better results have since been obtained with the method now in routine use. The advantage of subcutaneous over intramuscular injections is obvious, and the findings, if confirmed, will have applications far beyond the treatment of gonorrhœa.

Public Health Section

PROBLEMS OF INDUSTRIAL HEALTH IN INDIA

By S. CHAKRAVORTI, L.R.C.P. (Lond.), M.R.C.S. (Eng.)
Staff Medical Officer, I. C. I. (India), Ltd.
London

A WELL-PLANNED growth of Indian industry with adequate safeguards against disastrous fluctuations in the prices of primary goods would do much to raise the standard of living, helping to eliminate that appalling poverty which crushes millions of Indian people. The publication of the 'Bombay Plan' (Plan of Economic Development for India, 1944, 1945), the recent visit of the leading Indian industrialists to the United Kingdom, and the statement on industrial policy by the Government of India have aroused new hopes of greater industrial employment and increased productivity. The principal objective of the Bombay Plan is 'to double the *per capita* income of the Indian people within a period of 15 years'. The authors of the plan envisage that this can be achieved, even allowing for an increase in population of 5,000,000 per year, by so organizing the country's resources as to 'raise the output of agriculture to about twice the present figure and that of industry to at least five times the present output'.

Distribution of population

Out of a total population of about 400 millions, nearly 340 millions still live in the villages (there are some 700,000 villages in India) and rely predominantly on primitive agricultural means or simple 'cottage industries' for their livelihood, and in most villages pressure of this large population on the soil has already become intolerable (figure 1). Of the 50 million people living in built-up areas and cities not more than 20 million are engaged in or dependent on industry for their living, mostly in concerns of 20 or less, and of these less than $2\frac{1}{2}$ million people (i.e. 0.6 per cent of the total population) can be regarded as employed in large scale and *regular* industrial establishments.

Nature of principal industries and numbers employed

The industries in India fall into two classes—organized and unorganized. An industry is regarded as organized if it employs 10,000 persons or more in establishments containing not less than 10 persons in each and includes some of the important textile mills, iron and steel factories, mines, railway workshops, dockyards and plantations. The unorganized industries form the larger group embodying the numerous handicrafts which are carried on in cottages and small workshops (employing less than 10 persons) and their importance lies in the fact that they are the indigenous industries of India and give employment to a far larger number of

workmen than the organized industries (Blunt, 1938).

The factories in India are divided into two groups: (a) *regulated*, where 20 or more persons are employed and mechanical power is used in any part of the manufacturing process, and (b) *unregulated*, where mechanical power is not used and less than 20 persons are employed, but in certain circumstances any premises in which 10 or more workers are employed can be declared as a 'regular' factory whether power is used or not (Indian Factories Act, 1934, Amendments 1936, 1940, 1941).

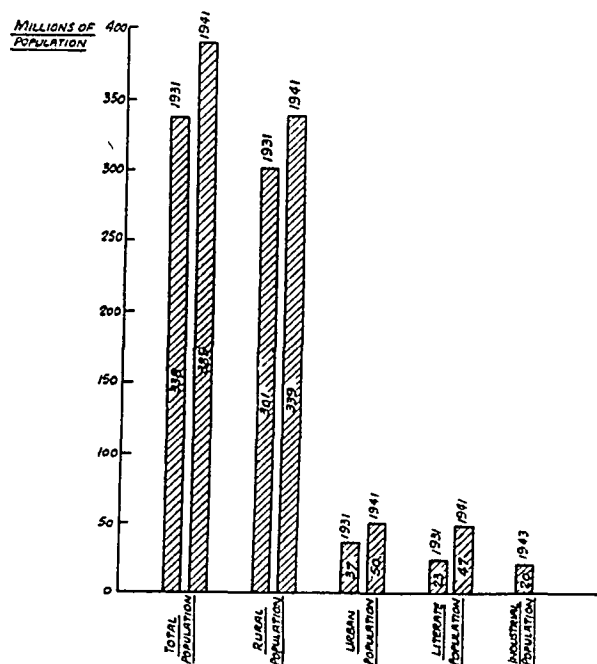


Fig. 1.—Showing India's population variation in the decade 1931-41.

(Compiled from:—*Indian Year Book*, 1943-44.)

The regulated factories are again subdivided into two classes—the seasonal and the perennial or non-seasonal. A seasonal factory is open for less than 120 days in a year and deals only with agricultural products as these become available, for example, cotton ginning, cotton and jute pressing, and the manufacture of coffee, indigo, rubber, sugar, tea, etc.

In 1942, for which the latest figures are available, the distribution of these two classes of factories was as follows (Statistics of Factories, 1944, Government of India):—

	Number of factories	Number of workers employed
Seasonal	3,681	301,551
Perennial	8,846	1,900,879
	<u>12,527</u>	<u>2,202,430</u>

The textile industry.—Cotton is one of the most important commercial crops in India. In 1940-41 the average area under cotton was 23.6 million acres with a yield of 5.9 million bales of 400 lb. each, of which some 2.9 million bales were exported.

In 1942 there were 396 mills operating, employing about 480,447 workers.

The jute industry.—The total number of jute mills in 1939 was 107, employing some 290,000 workers. Of the total average output of 1.2 million tons India consumes only 20 to 25 per cent, the rest being exported.

The iron and steel industry.—This industry, barely 35 years old, occupies a key position among the industries in India. The first successful attempt at manufacturing steel on a modern scale was launched by the Tata Iron and Steel Co., and it has since enjoyed an unrivalled supremacy. With a capital investment of nearly Rs. 25 crores* (approximately £13,750,000) the company also owns valuable iron and manganese concessions, and limestone, coal, dolomite, magnesite and chromite deposits scattered all over India.

It employs some 150,000 workers and it has been stated that, including their dependants, the total number of people supported by this company is in the neighbourhood of 600,000.

Mines and quarries.—There are some 150,000 persons employed in coal mines and approximately 120,000 work underground. The production of coal in 1939 was over 28 million tons, valued at Rs. 10 crores (£7,500,000). Indian coal seams are, by the way, much thicker than those in Britain. Many of the seams are 7 to 10 feet high, thus enabling a miner to stand upright at his work for most of the time. On the other hand, most seams of good-quality coal in India give off much fire-damp. This, together with coal-dust, is often responsible for serious explosions and fires in the mines. Furthermore, the pillars that are left are generally inadequate to support the remaining coal with the result that premature collapse and sudden subsidence are frequent, and lives are lost both below and above ground.

The other minerals which are extracted in India, namely gold, silver, copper, manganese, mica, petroleum, salt, saltpetre and gypsum, etc., give work between them to some 100,000 persons.

The number of fatal accidents in the mines during the year 1942 was 287; in addition some 10,871 persons received minor injuries which necessitated enforced absence from work for a period exceeding 48 hours. The average death-rate from accidents per 1,000 employees was 1.27 for the period 1929-37. There are some 40 permanently burning fires in 22 different

collieries (Reports of the Chief Inspector of Mines, 1935-42, Government of India).

Railways.—Indian railways extend over 40,470 miles and employ a staff of about 800,000 workers. The railway administrations form some of the largest employers of organized labour. About 45 per cent of the total mileage is managed by the government executives and the remainder by private companies which are mostly formed in England. Their policies in respect of wages and other problems vary in different parts of the country and the systems of ownership and management are highly complex (Anstey, 1936)*.

Plantations.—There are large plantations of tea, coffee, sugarcane, tobacco, rubber and some cinchona. Of these, tea is most important as it is one of the principal items of Indian export. In 1940, the total area under tea crop was 833,000 acres, yielding over 464 million pounds. Nearly 920,000 persons are employed in tea plantations and associated factories. Although India produces large quantities of tea, its home consumption is comparatively little, being of the order of 106 million pounds per annum; the surplus is exported to other countries, principally to the United Kingdom.

Coffee plantations employ about 99,000 workers, and some 150 sugar refinery factories situated in different parts of India between them employ about 125,000 persons.

The opium trade.—Contrary to popular belief, India is not an unscrupulous producer or consumer of this sinister drug. According to the League of Nations' findings 'the misuse of opium is a negligible feature in Indian life; abuse of its properties is rarer in India than the abuse of alcohol in the Western countries' (*Indian Year Book*, Bombay, 1943-44, 30, 715).

The total area of cultivation has been methodically reduced from 27,228 acres in 1932 to about 4,819 acres in 1941, and the Government of India has taken steps not only to cut down the home consumption to a gradual extinction but also to prohibit export of this drug except for exceedingly small quantities for medicinal and scientific purposes.

Hours of work

With certain exceptions, the Indian Factories Act of 1934 stipulated that the hours of work in perennial factories should be limited to 10 hours per day and 54 hours per week, and in seasonal factories to 11 and 60 hours respectively. Most organized industries normally work a uniform 10-hour day from Monday to Friday, and 4 or 5 hours on Saturday. In certain industries,

* All monetary calculations in this paper are taken as Re. 1 equivalent to 1s. 6d. One lakh is hundred thousand rupees, and one crore is ten million. At the present rate of exchange these are equal to £7,500 and £750,000 respectively.

* The up-to-date figures kindly supplied by the C.M.O., E.I.R., are as follows: Total mileage of all railways in India is 40,944, of which 32,967 is under State control, 6,818 is under Indian States and 1,159 under private companies. Total number of railway employees on all railways on 31st March, 1945, was 962,009.—EDITOR, I.M.G.

especially cotton spinning and weaving mills, a 60-hour week is permitted provided that the additional 6 hours over the 54-hour week are paid at overtime rates. In dockyards and railway workshops anything from 48 to 54 hours per week is the general practice. The Act further makes it compulsory that ordinary trading shops (restaurants and places of amusement excepted) shall close not later than 9 p.m.

No special provision has been made in the Act governing hours of work of women employees; and there is nothing to prevent employment of women on night-work, or in mines and docks. The Act forbids, however, the employment of children (9 to 12 years, and in some specified trades up to 15 years) between the hours of 7 p.m. and 6 a.m. (Employment of Children Act, 1938).

Average income

A worker, whether on land or in industry, receives very low wages of which the following are examples :—

Occupation, men over 21	Daily wages for 10-hour day	Averages daily wages in Britain for 8½- hour day
	Rs. As. P.	s. d.
Agricultural labourers ..	0 2 3 (3d.)	10 0
Miners ..	0 8 0 (9d.)	16 6
Unskilled workers in industry ..	0 7 1 (7½d.)	12 0
Skilled workers in urban industries such as textile mills, engineer- ing workshops, etc., up to ..	1 5 0 (1/11d.)	17 0

Women's wages are unbelievably low, about half that of men, and thousands of children are often employed in sedentary occupations at 1 anna 3 pies (2d.) per day, sometimes working for 10 to 12 hours (Barstow, Davies and Sloan, 1942).

Grigg (1938), on behalf of the Government of India, estimated that the *per capita* average annual income was in the neighbourhood of Rs. 56 (£4 4s.). Towards the end of 1942, however, partly due to wartime exigencies, the earning capacity of an ordinary worker had improved considerably, and taking an average of all industries, the following can now be accepted as typical samples of monthly income :—

Monthly wages			
Adult male ..	Rs. 14 to 30	(21s. to 45s.)	
Adult female ..	Rs. 10 to 20	(15s. to 30s.)	
Children ..	Rs. 7 to 12	(10s. 6d. to 18s.)	

Nutrition and deficiency diseases

On their meagre earnings Indian workers cannot afford a well-balanced diet. Aykroyd

(1937) in his survey of nutritional problems in India showed that in pre-war days the cost of obtaining the minimum subsistence diet, inadequate and ill-balanced, consisting of cereals and very little else, came to at least Rs. 2-8 a month (4s. 3d.); a reasonably balanced diet, judging by Indian standards, cost between Rs. 5 and 6 a month (7s. 6d. to 9s.). He further estimated that in normal times about 30 per cent of the population were *quantitatively* underfed, and at all times the quality of the diet suffers more than the quantity.

In recent years, especially since 1940, the cost of living has been rising out of proportion to the standard of income. The average diet is almost completely devoid of animal proteins, fats, vitamins A, C and B₂ groups, calcium and other minerals, and thus accounts for the inevitable under-nutrition of the population as a whole. The average daily caloric intake for a working adult amongst the poorer classes is between 1,700 to 1,800 (Aykroyd, 1944). Between 30 and 40 million people do not have more than one meal per day and virtually live on the level of starvation. About 88 per cent of the families' budgets contain no reference to milk or its by-products; the average consumption of fluid milk for the whole population is estimated to be less than 2 ounces per day. At schools 6 out of every 10 children suffer from malnutrition. Dietetic deficiency is also responsible for nearly 2.5 million cases of rickets and some 3 million cases of night-blindness, and it is said that for every one blind there are three partially blind in India. Sorsby (1945), in a comprehensive survey of the incidence of blindness in the British Commonwealth, thought that the correct figure for India would be between 10 and 15 million cases.*

This defective nutrition, quantity taking precedence over quality of the food, is also responsible for the poor physique of the masses, and the lowered resistance to many diseases such as tuberculosis (341,659 cases were reported in 1939); cholera (200,000 deaths annually and many times more during epidemics); smallpox (48,104 deaths in 1939); malaria (over 1 million deaths annually); leprosy (present incidence known to exceed 2 million cases); and thousands of cases of anæmias of pregnancy, to name only a few of the more important ones. For every person suffering from obvious disease there are many whose health is impaired from lack of energy-building and protective foods (Annual Reports of the Public Health Commissioner, Government of India, 1939-42). It is, however,

* Probably there are many more cases than recorded, for data are not always obtained from hospitals and dispensaries, while many suffer and die in silence in the village. Similarly the vital statistics in India are often grossly inaccurate; in urban areas these are collected by the municipal authorities but in rural districts it depends on the reports made by the village headmen and lay officials who are usually illiterate as well as uninterested in their task.

useless to tell these people to drink more milk or eat more fruits and vegetables unless these articles can be made available to them *in addition to* and not *instead of* part of their usual diet. 'To suggest expensive food to these people would be just as reasonable as the remark attributed to Queen Marie Antoinette who, when told that the people of Paris were clamouring for bread, was said to have replied, 'If they have no bread, why don't they eat cake?' (Blunt, 1938).

Housing and rent

The bulk of the workers, whether on plantations or in industry, live in one-room tenement huts or chawls, 6 feet by 9 feet, and mostly several persons in a room. In some cases a small allotment of land is offered with these huts where the inhabitants can grow vegetables for domestic consumption. The rents are high compared to the accommodation and wages of the workers. Average rentals for such tenement huts vary from Rs. 2-10 to Rs. 5-5 (4s. to 8s.) per month. This necessitates more than one family sharing a single-roomed tenement, and in such rooms 'the occupants cook, eat, sit and sleep and at times also deliver babies' (Khandwallah, 1938).

In Bombay City (population $1\frac{1}{2}$ million) the living space in industrial areas is about 28 square feet per person and it has been estimated that in this province generally the number of inhabitants was 124 per acre in 1943. This may be compared with the industrial congestion of such cities as London (54 per acre), Liverpool (27 per acre), and Sheffield (13 per acre).

Overcrowding is so acute in the principal industrial areas that thousands of people sleep on the city streets and pavements (Morris, 1945).

Factory welfare, workmen's compensation and trade unions

Social services in the factories, and in the country generally, are very meagre. Except for some compensation in the event of death or permanent total disablement from industrial hazards and accidents, there are no national unemployment schemes, or sickness or other benefits, no insurance schemes, and no pensions.

Factory welfare.—Section 33 of the Indian Factories Act makes it obligatory for all factories employing over 150 workers to provide adequate shelters for the use of workers during periods of rest. Apart from this a number of modern industrial establishments in India do provide 'tiffin rooms' and rest shelters for their work-people and many of them have also established 'tea stalls' on the premises. There has been very little effort made, so far, to run co-operative canteens on lines such as are known in Britain. Some pioneering work in this direction, however, has been done by Messrs. E. D. Sassoon & Co. in Bombay. This firm owns nine large cotton mills in the city and manages 'canteen' facilities at each mill. The

company bears the salaries of the staff and cost of equipment, and hot meals are provided for the workers at actual cost price. The Tata Iron & Steel Co. maintains a number of 'restaurants' at their various works which supply cooked meals and refreshments to the workmen at cost price. The company has its own plant for the manufacture of ice and soda water which are provided free of charge to their employees. There are also 'rest houses' where women employees can wash and change; and a 'nursery' where they can leave their babies to be looked after while they are at work, these babies being supplied with milk and biscuits free of charge.

Many other labour-employing organizations, such as the Indian railways and the Calcutta and Bombay Port Trusts, also provide safety and welfare facilities in their various workshops but these are not uniformly good. 'All this is, however, but a drop in the ocean and the vast majority of employees in India have no welfare schemes of any kind at all' (*Indian Year Book*, Bombay, 1943-44, 30, 501).

Workmen's compensation.—Compensation is paid only in cases of death or injury causing permanent disability, and for certain specified industrial diseases such as lead and phosphorus poisoning, arsenic poisoning, benzene poisoning, caisson disease, chrome ulceration and primary epitheliomata of skin. The scale of compensation varies from Rs. 500 to Rs. 4,000 in case of death (£37 5s. to £300), and for permanent total disablement the figures are now from Rs. 700 to Rs. 5,600 (£52 10s. to £420). The rates for temporary disablement from industrial poisoning are very low, but it is stated that the Workmen's Compensation Act, 1923, Amendment 1939, at present covers about 6,000,000 workers in all industries. The amount of compensation paid during the war years is not published, but it is known that during a period of 15 years (1924-38), the total amount of compensation paid was over Rs. $1\frac{1}{2}$ crores (£125,000) in over 280,000 cases.

Trade unions.—Backward as social conditions are, however, the Indian workers have built up a trade union movement which shows a remarkable record of struggle and achievement. The earliest trade unions were the Bombay Millhands Association, formed in 1890, and the Amalgamated Society of Railway Servants which was founded in 1897. These were rather weak organizations, more like 'friendly societies' than unions for seeking concessions and ventilating grievances. After the first world war rapid progress was made by the trade union movement, led by many honest and genuine leaders, and to-day, with a membership of over 600,000, the organization has a strong representation both at the centre and in the International Labour Organization.

The Trade Unions Act of 1926, Amendment 1928, was an important gain in the history of the movement. Unlike Britain and other European countries, the Act applies only to those unions which seek registration under it,

the registration being voluntary. It confers on the unions and their officers a certain measure of immunity from civil and criminal prosecutions. The investigation and settlement of trade disputes are governed by the Trade Disputes Act of 1929, Amendment 1938. The machinery which it provides is of the nature of a 'court of inquiry and conciliation' with rights of entry and inspection of work-places. India has also been closely linked with the International Labour Organization from its inception, and at present occupies a permanent seat on the governing body of that institution.

Many trade unions, apart from securing concessions from employers and settling grievances, also provide a variety of welfare schemes in the form of dispensaries, facilities for education and recreation, co-operative stores and cheap grain-shops used for the benefit of their members. Nevertheless, trade unionism in India has not yet grown to anything like the extent to which it has been developed in the West. Fear of victimization and fundamental ignorance still prevent the workers entering into combinations promoted to safeguard their own interests, but things have taken a turn for the better in recent years.

Present health standards

Statistics of health and mortality which are collected and published in India relate to the whole community (see figures 2 and 3) and with the sole exception of accidents in factories 'no statistics are compiled separately for industrial workers alone'. In the absence of necessary data it is not possible to generalize on matters of industrial health and sickness or toxic hazards of occupational origin.

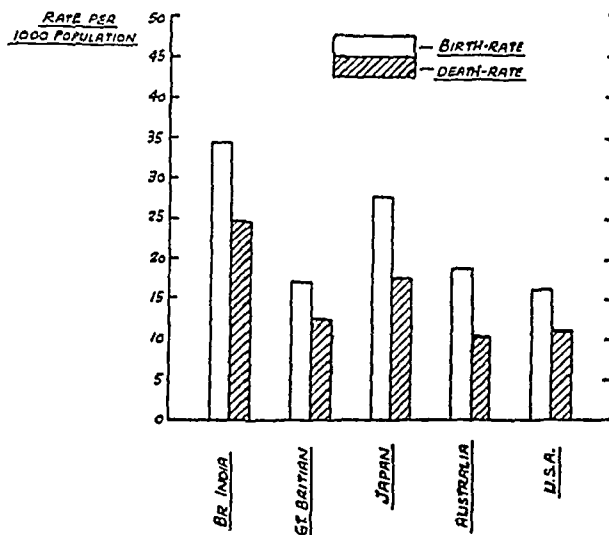


Fig. 2.—Some national birth-rates and crude death-rates per 1,000 population (1939).

(Compiled from :—Social Service in India. Sir Edward Blunt, 1938. *Lancet*, 1945, i, 743.)

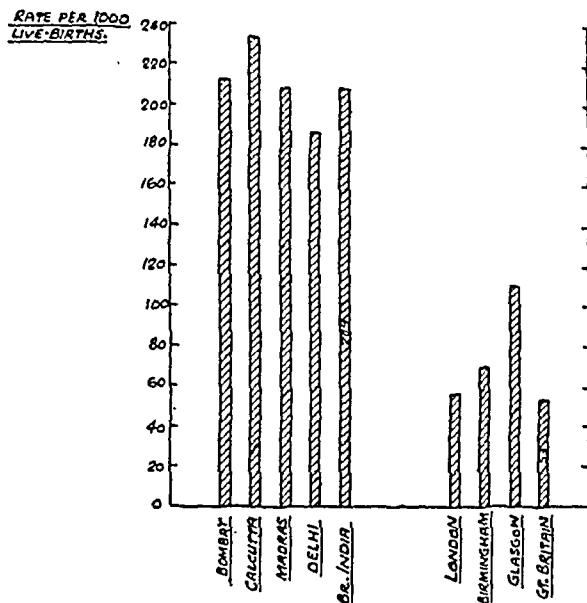


Fig. 3.—Infant mortality rates in some great cities (1941).

(Compiled from :—*Indian Year Book*, 1943-44. *Lancet*, 1945, i, 743. Social Service in India. Sir Edward Blunt, 1938.)

Accidents.—The figures for 'accidents in factories' for 1942 are as follows* :—

Type of accident	Perennial factories	Seasonal factories	Total for the year
(1) Fatal	276	47	323
(2) Serious (causing permanent disability).	8,799	312	9,111
(3) Mild (causing enforced absence from work for over 48 hours).	43,790	950	44,740
TOTAL	54,174

From this it will be seen that the accident rate is high; about 1 in 406 workers in Indian factories sustains physical injury in course of his work; 1 in 6,818 meets with his death. Many of these industrial accidents can be avoided by adequate guarding and fencing of the machinery as outlined in the Factories Act, but it has been the experience in Britain that 'however well machinery may be guarded by law, not more than a 10 per cent reduction in the accident rate can be looked for by the provision of safeguards alone' (Hunter, 1945).

Pre-employment medical examination of prospective employees, a carefully planned system of allocation into suitable types of work, 'finding the job for the man and the man for

* These figures do not include accidents in mines.

the job', and finally educating the workers to become 'accident-conscious' are measures which will help reduce this high accident rate in the factories.

General health.—The standard of health in India is low. Both the birth-rate and crude death-rate are approximately double that of Britain. The high birth-rate, however, is to a very large extent neutralized by heavy mortality both of infants and mothers at child-birth. The infant mortality rate in 1941 was estimated to be about 209 per thousand live-births and the maternal mortality rate was in the neighbourhood of 24.5 per 1,000 live-births; the corresponding figures for Britain were 53 and 4.1.

Grant (1943) estimated that the mean-age in India was 23.2 years as against 30.6 in England and Wales, and the expectation of life at birth was about 27 years in contrast to an expectation of 67 years in Australia, of 63 years in Great Britain and Germany, and of 47 years in Japan. Hill (1944) at a recent debate on 'India' in the House of Commons summed up the situation as follows :—

'The average new-born child in India has an even chance of living to 22; in Britain and America the same child has an even chance of living to nearly 70. This is not, as is commonly supposed, solely a matter of high infantile death-rate; it is due to a mortality which is four to eight times higher than ours right up to the age of 55. Corresponding to this high mortality sickness is widespread, with consequent inefficiency, poverty and misery. Nutrition, also, on any reasonable standard is for the most part appallingly low. No doubt there are tens of millions of people who are well-fed, but there are hundreds of millions of people who are ill-fed, and even among those who are comparatively well-fed the standard is much lower than we ourselves would tolerate'.

Only a rise in the standard of living, of comfort and proper education, can bring about any substantial improvement. All effective forms of propaganda through the press, posters and pamphlets, lectures and demonstrations must be employed for the diffusion of useful knowledge to the masses. The cinema and the radio too, properly directed, will play a vital part, for the illiterate is sometimes very quick to grasp what he can see and hear.

What is the next step?

India stands to-day on the threshold of an industrial revolution. Her potential resources for development are great, but with her present underpaid, under-fed, badly housed and unhealthy population, the outlook is disconcerting. While it is high time that more and more people were brought in to play their part in the industrial life of the country, so far there has been little evidence to show that Indian industrial organizations as a whole are applying, on any demonstrable scale, the results of research into the 'human problems of work'.

The industrial worker is as important as the machine, and the 'health protection of the man who works' is an essential pre-requisite to any manufacturing project (Wampler, 1943). The fact that ill-health of the worker causes not only a loss to industries but is an ultimate drag on the nation has come to be appreciated by comparatively few organizations, for, unfortunately, so long as labour is so cheaply obtained in India, the employer finds it an easier task to replace the worker who has taken ill rather than investigate and remove the cause.

As already stated the social services in India are very meagre and do not meet the requirements of the general public by a long way. There are some 42,000 doctors and only 7,000 qualified nurses in a country of 400 million people, averaging roughly 1 doctor to every 9,500 of population (Great Britain 1 to 776), and 1 nurse to nearly 57,000 (Great Britain 1 to 435). Three-quarters of the municipalities of British India are still without qualified health officers of any kind. There is no nation-wide provision for sickness, unemployment or old-age benefits. There is no Poor Law, and the lot of the worker at present is one of debt and destitution. Until some form of national scheme for disablement or relief for the unemployed is forthcoming, it is very necessary to ensure that the worker is at least maintained in good health during his 'working life' for his own sake and for the sake of the industrial progress of the country.

This, then, is a problem of grave magnitude; and it is a problem which has to be faced immediately and squarely if India is to avoid those heavy losses in men and material which accompanied the industrial revolution of the West, not so very long ago.

Conclusion

The object of this paper is to serve as an introduction to the problems of industrial health in India, and a plea for the promotion of industrial medicine alongside economic reconstruction and industrial development of the country to end poverty, ill-health and social backwardness.

Separate aspects of the hazards in industries such as fatigue, occupational poisoning, dermatoses, eye injuries, burns and shock have not been discussed owing to lack of data on these subjects.

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Current Topics

Care of the Filariasis Patient

By L. T. COGGESHALL

Captain, Medical Corps, U.S. Naval Reserve

(Abstracted from the *Military Surgeon*, Vol. 98, No. 2, February 1946, p. 89)

THE results attained in the treatment of filariasis in relatively lightly infected servicemen without the aid of curative drugs were conducted upon the broad generalization that it was a self-limited infection and as such should respond to a programme which promoted physical and mental fitness. That this assumption was justified is shown by the fact that it was possible to return all but 171 of 2,295 men to full and all duty, 85 per cent within the first four months after outset of the programme. None of the 171 men who were separated from the service for medical reasons were separated because of filariasis. The reasons for their disposition were primarily neuropsychiatric difficulties which existed prior to the acquisition of their filariasis.

An analysis of the problem at the present time shows it to be one of decreasing importance.

The dreaded complication of elephantiasis has not appeared in a single individual among the men observed on this post.

There has been no loss in any of the capacities concerned with the earning of a livelihood nor has there been any impairment in their reproductive functions.

Finally, a programme which has as its basic concept the promotion of physical and mental fitness has been eminently successful in the care of such an infection as filariasis which again emphasizes the importance of avoiding the pitfall of the 'abuse of rest' demonstrated conclusively in so many other disorders.

Gonorrhœal Syndrome without Gonorrhœa : Reiter's Disease

By ROBERT L. LUCAS

and

HARRY WEISS

(Abstracted from the *Journal of Venereal Disease Information*, Vol. 26, December 1945, p. 268)

REITER'S disease is defined as gonorrhœal syndrome of urethritis, conjunctivitis and cutaneous lesions without gonorrhœa. The disease can only be distinguished from gonorrhœa by repeated negative smears. The disease is milder and is followed by complete recovery. It fails to respond to sulphadiazine and penicillin

therapy. The cause of the syndrome as well as specific therapy for it remains unknown.

A. B. R. C.

A Case of Third-Generation Syphilis

By C. J. V. HELLIWELL

(Abstracted from the *Journal of Venereal Disease Information*, Vol. 26, December 1945, p. 269)

HELLIWELL describes a case of third-generation congenital neurosyphilis inherited from a congenital syphilitic mother showing a positive Wassermann reaction in blood but no signs or symptoms.

The patient had a typical tabetic gait with spasticity of the lower limbs and slight sensory loss in both feet. Wassermann reaction was strongly positive.

The father had been a blood donor and it is assumed that he was free from infection.

The patient improved considerably after neurosyphilitic treatment.

The writer concludes that closer investigation into the histories of congenital syphilitics might show the disease to be commoner than is supposed. He adds that most hopeless patients may be benefited by treatment. Further he asks whether cases like this could be avoided by administration of arsenic to all congenital syphilitics during pregnancy.

A. B. R. C.

Isolation of *Mycobacterium lepræ* in Culture

By R. ROW, D.Sc., M.D. (Lond.)

(Abstracted from *The Indian Physician*, Vol. 5, 1946, pp. 75-81)

THE common property possessed by the sera of patients suffering from leprosy and kala-azar of fixing complement in the presence of antigens prepared from acid-fast bacilli indicates the presence of a common antigenic factor in leishmania and acid-fast bacilli.

Dr. Row has taken advantage of this fact to cultivate the leprosy bacillus in symbiosis with leishmania, and claims to have succeeded in his efforts.

For making the primary cultures he used hæmoglobinized saline described by him as early as 1912 as a suitable culture medium for leishmania. The growth from this primary culture is transplanted on the surface of solid media. For this purpose Dr. Row has used solidified hæmoglobinized saline agar (described by him in 1930) and glycerinated potato. By this method he reports to have obtained pure cultures of *Myco. lepræ* and *Myco. lepræ muris*. The pure cultures are reported to be pleomorphic, which ultimately settle down into fine coccid forms with coccid-bacillary intermediary stages. All the forms are however acid-fast, and can be converted into bacillary forms by repeatedly growing them in symbiosis with leishmania. Sub-cultures are reported to be easily made from the parent cultures.

D.

Anaphylactic Shock from Skin Testing : Two Cases—One Fatal

By OSCAR SWINEFORD, Jr., M.D.

(Abstracted from the *Journal of Allergy*, Vol. 17, No. 1, January 1946, p. 24)

1. Two cases of anaphylactic shock from intracutaneous skin tests with food extracts are described. The food which caused the fatal reaction was not determined. The non-fatal reaction was thought to be due to mustard.



Highly Active Glycoside of *Digitalis Leaf*

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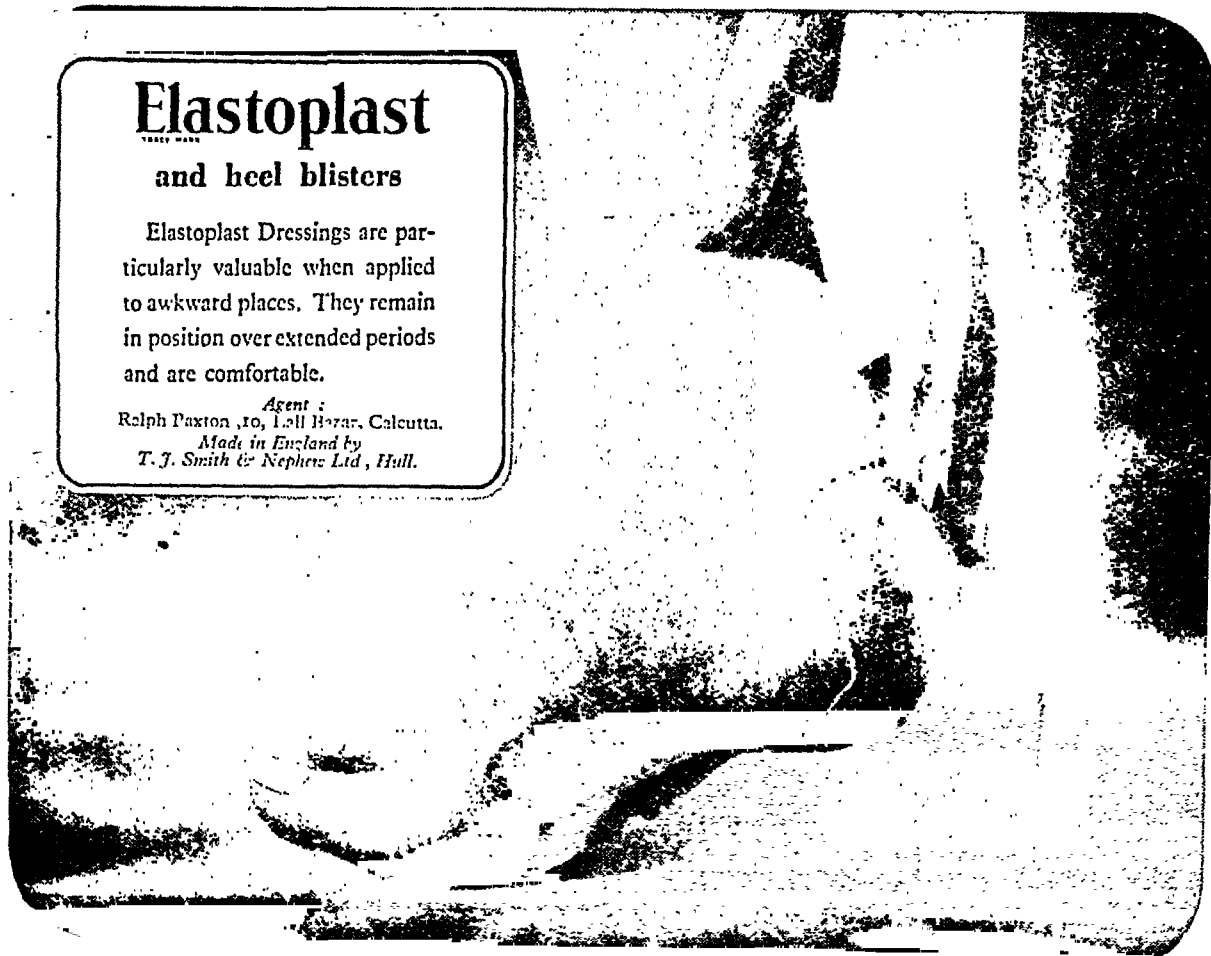
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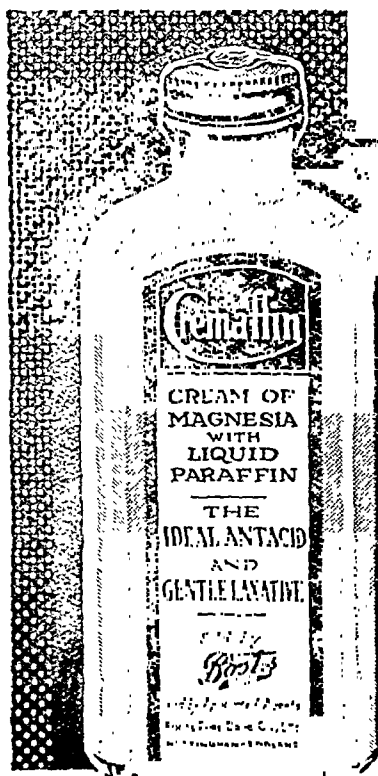
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2. In both, anaphylactic shock occurred before there was time for the skin reactions to become strongly positive.

The Problem of Post-Maturity

By A. J. WRIGLEY

(Abstracted from the *Lancet*, i, 6th April, 1946, p. 501)

THE writer is dissatisfied with the prevalent methods of diagnosis and management of post-mature cases.

The general assumption that if a pregnancy continued beyond the date calculated for its termination, the foetus would become so large as to cause difficulty at the delivery is, according to the writer, an erroneous idea. Prolonged pregnancy does not necessarily result in a large child.

The decision to terminate pregnancy should be dictated not by dates but by the foetal development as judged by repeated regular clinical examinations. In true post-mature cases repeated clinical examinations are necessary when concurrent with increased size would be found increased strength and tone, so that the foetus would become more rigid. As the amount of liquor amnii apparently does not increase in the last weeks of pregnancy the foetus becomes progressively more easily palpable—so easily that the uterine wall may be imagined to outline the foetal position and limbs.

In induction it should be a rule that if medical induction is justified there is also justification for surgical induction. Moreover, in repeated medical induction there are inevitable physical upheaval and anxiety at each failure.

The routine termination of pregnancy at fixed times such as 40th or 42nd week should be abolished, as three variations are possible:—

1. Labour might start days or weeks after the expected date and result in the delivery of a large post-mature baby.

2. A normal sized or even small baby may be delivered.

3. At about the calculated date the woman may be delivered of a large baby that showed every characteristics attributed to post-maturity.

The combination of physical signs found by repeated physical examinations should therefore be the guide for the course of action.

B. B.

Radiation Sickness in Nagasaki

By J. J. TIMMES

(Abstracted from the *United States Naval Medical Bulletin*, Vol. 46, February 1946, p. 219)

WHEN the atomic bomb exploded, the concentrated energy diffused itself in three main channels, namely, pressure, heat and radiation. The effects of the atomic bomb differ from the ordinary explosive bomb only in its release of radiant energy.

The Japanese stated that during the first week most of the deaths were the result of radiation sickness; however they did not differentiate blast victims from radiation patients. They also attributed to radiation many thermal burns. It can be assumed, however, that a large percentage of the early victims died of radiation effect.

Only a few cases which could be classified as x-ray skin burns were noted.

Many cases of alopecia were seen. Some of these victims began to lose their hair 4 or 5 days after the explosion, while others first noted this phenomenon about the third week.

The principal effect of the radiation was on the bone marrow, with a marked degree of depression of the marrow function. Most of the cases seen showed an aplastic type of anaemia. The blood was deficient

in red blood cells and haemoglobin, but was not markedly hypochromic. As granulopoiesis was greatly impaired, agranulocytosis resulted. A lymphocytosis existed, but seemed to be of a relative nature. A number of white blood cell counts under 1,000 were seen and in some of the cases the white blood cells completely disappeared before death. A white blood cell count under 1,000 offered a poor prognosis; however one patient with 400 cells per cu.mm. recovered. Although platelet counts were not made, smears showed a great decrease in the number of thrombocytes, and in some of the smears they had completely disappeared. Petechiae were commonly seen, as were gross haemorrhages. Bleeding times were increased and often were found to be prolonged over 45 minutes. Jaundice was not seen, but all of the patients showed a marked degree of pallor of the mucous membranes. The liver was found slightly enlarged in only one case, and the spleen was not enlarged in any case. Urine analysis frequently revealed albumin, casts, bile, and red blood cells.

The average newly admitted patient complained of fever, malaise, loss of appetite, bleeding gingivae, and haemorrhagic diarrhoea. Examination revealed generalized petechiae, alopecia, various buccal lesions, and the blood picture of aplastic anaemia.

The oral changes consisted of a glossy, smooth tongue, with ulcerative lesions of the mucous membranes. The ulcers were composed of necrotic areas with a complete clinical absence of a surrounding inflammatory zone. The lesions bled easily, were often grossly infected and showed no tendency to heal. Two cases of necrosis of the mandible were seen and one case of noma with ulceration of the lips and necrosis of the mandible and maxilla. The teeth were generally loose and easily removed by hand.

Many of these patients died as a result of terminal infection, particularly broncho-pneumonia.

Opportunities for therapeutic endeavours were necessarily handicapped by our limited supplies.

Penicillin and plasma had the anticipated beneficial effects. The one case of noma responded particularly well, in that the patient was converted from a critical status and was placed on the road to recovery within 2 days. Liver extract seemed to benefit a few patients, but in general was not very effective. Pentnucleotide was used in limited amounts, namely, 3 c.c. three times daily, in seven cases, and in each one of the patients a progressive rise of the white blood cell count appeared in 24 hours. Only one patient on whom pentnucleotide was used had a white blood cell count under 1,000, and the remainder were under 2,000. Some of the patients who acquired infections would respond with a leukocytosis.

Reactions to Penicillin

(From the *Lancet*, i, 2nd March, 1946, p. 316)

ONE of the remarkable features of penicillin therapy has been the rarity of reactions, but two articles in this issue demonstrate the troublesome reactions are not unknown. How far these are due to impurities must remain doubtful until pure penicillin is generally obtainable. Commercial penicillin now contains some 30 per cent of impurities, whereas in the early days it contained 80-90 per cent, and increasing purification has certainly made reactions increasingly rare. Even now, however, Cormia and others have encountered reactions severe enough to necessitate the discontinuance of penicillin therapy in 0.5 per cent of 2,000 U.S. soldiers given long courses of the drug for various infections. Reactions to penicillin—like those to the sulphonamides—may appear either soon after administration begins, where the patient is 'naturally' hypersensitive or has been sensitized by a previous course of penicillin, or some days later when the patient has acquired sensitivity during the course of treatment: commonly, as in the cases reported by Major Haswell and Captain Wilkinson, the reaction will then appear, like serum-sickness, after administration has ceased.

It seems fairly certain—though the result of skin-tests are not conclusive—that penicillin itself can produce a contact dermatitis after protracted application. Pyle and Rattner and Barker described cases in doctors and orderlies who had been making up penicillin solutions for a long period; patch tests with crystalline penicillin were positive in Pyle's cases. Cormia and his colleagues report a case of severe urticaria with angioneurotic oedema, leading to pulmonary oedema, beginning 24 hours after the local application of penicillin ointment in a soldier who had received two courses of parenteral penicillin in the previous month; these had presumably produced sensitivity. Of the reactions produced by intramuscular injection by far the commonest form is urticaria; among the 209 surgical cases treated with penicillin by Lyons in 1943, urticaria sometimes accompanied by fever and abdominal colic, developed in 5.7 per cent. Cormia and his colleagues also mention a reaction resembling serum-sickness; also acute syncope, transient miliaria-like eruptions, erythematovesicular eruptions at times simulating dermatophytosis, erythema nodosum, and epididymitis. They give one example of epididymitis arising in the penicillin therapy of early secondary syphilis and quote the 10 examples of epididymitis which Rosenburgh and Arling encountered in 65 cases of meningococcal meningitis treated with penicillin. From a small study with intradermal tests they conclude that fungus diseases of the skin predispose to penicillin reactions.

Lyons takes the view that urticarial reactions are so transient that they can usually be ignored and penicillin therapy continued in spite of them; this can hardly apply, however, where there is a severe general reaction. Macey and Hays have obtained good results in severe reactions with intravenous infusions of 50 c.cm. of 50 per cent dextrose solution.

Lightning Injuries

(Abstracted from the *Lancet*, i, 9th March, 1946, p. 351)

LIGHTNING injuries are manifold. These injuries are more common than is usually realized, but the number of deaths is small in proportion to injuries which may be in the form of burns, fractures, lacerations, cataracts, and various lesions of the nervous system.

Burns are the most common injuries from lightning. They may produce unusual patterns, such as arborescent markings on the skin and long narrow lines. The force of explosion may cause large lacerations. Ashby described the unusual case of 3 children who developed left-sided alopecia a fortnight after they were struck by lightning; their hair grew again after six months. The electric lesion, however, is not a true burn; it is painless and without inflammatory reaction. Vasoconstriction and vasoparalysis with subsequent thrombosis account for the pathological effects. This view is important in the treatment of these 'burns', for which Jellinek recommends masterly inactivity. Bleeding from the ear followed by unilateral deafness has been reported. Affections of the eyes include conjunctivitis and accommodation paresis, but cataract is more frequent. Effects on the central nervous system are divided into three groups: (1) immediate, comprising shock, unconsciousness, and 'suspended animation'; (2) secondary, including visual disturbances and temporary nervous disorder; and (3) remote effects including various rare complications.

A person struck by lightning usually falls unconscious at once. Retrograde amnesia is common. Among the secondary effects, flaccid paralysis of the lower trunk and of the legs is the most outstanding, and objective sensory disturbances also occur. The condition is temporary, power and sensation usually returning to normal after 12 hours. Next in frequency are hysterical manifestations—hysterical deafness, blindness, and loss of speech. Late changes may take the form of 'spinal atrophic paralysis', which consists in muscular atrophy with fibrillation, without sensory disturbance, in the distribution of the 4th, 5th and 6th cervical segments of the cord.

The knowledge of what to do in a thunderstorm is particularly important in open country, on mountains, and in the tropics. It is safest to be inside a house, in a room with all the doors and windows closed, and away from the fire-place. Telephones fitted with lightning arresters may be used without danger. The main switch and meter of the electric-light supply, however, should be avoided. The lead-in wire from the aerial to a wireless set should be earthed. If there is no house, shed, cave, or closed motor-car available, the protection of a ditch or hollow should be sought. Crowds of people and the neighbourhood of domestic stock should be avoided, as should trees standing alone, wire fences, hedges, walls, and the banks of rivers and ponds. The centre of a wood is fairly safe. In the mountains it is well to be away from peaks, lone rocks, and other exposed spots. If one is to be struck it is better to be wet through, for wet clothing or even skin may short-circuit most of the current.

People struck by lightning, unconscious and apparently lifeless, should be treated by artificial respiration without delay. This should, if necessary, be continued for up to eight hours, and Silvester's or Eve's method is to be preferred because it is important to watch the patient's face and neck for the 'deglutition phenomenon'. According to Jellinek, swallowing is the most reliable sign of the return of spontaneous breathing. When it starts it is imperative to stop artificial respiration at once.

Dental Emergencies and the Medical Practitioner

By F. C. WILKINSON

(Abstracted from the *Practitioner*, Vol. 156, March 1946, p. 160)

TRAUMA AND HÆMORRHAGE FOLLOWING EXTRACTIONS

THE extraction of teeth is frequently followed by a capillary oozing that lasts for several hours. Too often, unfortunately, in the early hours of the morning, patients or their relatives get alarmed at what appears to be a serious loss of blood. They fail to realize that the bulk of the fluid expectorated into a bowl is but blood-stained saliva. So the practitioner is urgently summoned. He arrives to find a patient with a mouth full of blood clot and a slight trickle of blood, but the pulse is full and there are no general signs of the loss of blood. He is not impressed, but something has to be done to reassure the patient.

The first step is to wash out the mouth and get rid of any blood clot, and then ascertain the site of the bleeding. A spray, with some force behind it, is needed, and a Higginson's syringe can be used for the purpose. A solution of eusol or Milton can be used with advantage. Pressure should then be applied to the bleeding part and maintained for at least ten minutes. The patient can do this by biting on a pad of cotton-wool placed between the jaws. The pad can be saturated with full-strength eusol, which, apart from its antiseptic properties, does seem to accelerate clotting.

In the absence of some specific blood dystrophy, this should suffice, but the patient should be warned to refrain from disturbing the clot by keeping the tongue away from the site and by not rinsing the mouth for several hours.

Occasionally, hæmorrhage may be due to some blood deficiency that produces a prolonged bleeding or clotting time. In cases in which the loss of blood is of some significance, this possibility can be checked by pricking the lobe of the ear and placing a drop of blood on a slide, or any odd piece of glass, and noting the time a clot takes to form. The immediate treatment is the same: apply pressure to the bleeding part. In cases in which some defect in the patient's blood markedly prolongs the clotting time, the only adequate remedy is to give the patient a transfusion of plasma or whole blood. Such a condition should, of course, have been ascertained before the operation. The use of styptics is of doubtful value, and when apparently successful, the result is probably due to the pressure applied.

The Sulphonamides : Present Place in Therapeutics

By J. S. LAWRENCE

(Abstracted from the *Medical Press and Circular*, Vol. 215, 13th February, 1946, p. 110)

SULPHAMEZATHINE, because of its low toxicity, is a valuable compound for routine treatment of both systemic and urinary infections. It rarely causes nausea or vomiting, and being readily soluble in the urine, both in the free and conjugated form, it does not readily form crystals, and does not therefore give rise to obstruction of the renal tubules or ureters. This is a valuable feature when treating dehydrated patients passing small amounts of highly concentrated urine.

Sulphadiazine, like sulphamezathine, is remarkably free from toxic symptoms, but has a low solubility in the urine, and is therefore liable to crystallize, causing hæmaturia and suppression of urine. It should be avoided in dehydrated patients or those in whom an ample urinary output cannot be assured. It has, however, little tendency to combine with protein in the plasma, and a large proportion of the plasma content is therefore in the free or active state, passing readily into the cerebrospinal and tissue fluids. Sulphadiazine is thus indicated particularly in meningitis.

Sulphathiazole is the most potent sulphonamide in present use, but is more toxic than those so far considered. It is apt to cause nausea and vomiting, and drug fever and eruptions often arise. As it is excreted very rapidly by the kidneys, high blood levels can be maintained only with difficulty. It should, however, be used in severe infections or when the response to the less potent sulphonamides is inadequate, but must be given in large doses. As with sulphadiazine, an ample urinary output is essential, for the conjugated form is very insoluble and readily forms crystals.

Succinyl and phthalyl sulphathiazole are practically unabsorbed. As they pass down the intestine they slowly liberate sulphathiazole. They are thus of low toxicity and can be used in high dosage. They are employed to lower the coliform count in the stools in anastomotic operations on the colon and in the treatment of dysentery carriers.

Sulphamerazine is rapidly absorbed from the intestine, but is excreted very slowly. Consequently, frequent dosage is not required, a valuable feature in prophylaxis, as, for example, in the prevention of streptococcal sore throats in rheumatic children or to protect contacts during an epidemic of cerebrospinal fever. In such instances it is sufficient to give one tablet 12-hourly.

Sulphacetamide is very soluble and of high penetrative power, particularly the sodium salt, which, unlike those of the other sulphonamides, is but weakly alkaline and capable of being made neutral without precipitation. It has been used particularly for eye diseases, and when applied as a concentrated solution, will penetrate into the anterior chamber and iris. It also penetrates the skin more readily than the other sulphonamides when applied as a cream. Because of its ready solubility in urine, sulphacetamide has been used in urinary infections, but is less potent than sulphamezathine for this purpose.

Sulphanilamide, being fairly soluble and having little tendency to cake, is particularly suitable for local application to the peritoneum and pleura and to wounds and burns. Owing to its low potency it should not be used for oral treatment in any but the most susceptible infections, and, even in these, undesirable toxic effects make it less desirable than sulphamezathine. Homosulphanilamide (Marfanil) is also used (generally mixed with sulphanilamide) as a local application for wounds. Unlike the other sulphonamides, it is active in the presence of pus and necrotic tissue. It has a greater bacteriostatic action against *Cl. welchii*, and should therefore be included in any sulphonamide mixture used for the treatment of wounds, particularly if gas gangrene is suspected. Being very rapidly excreted, it is unsuitable for systemic use.

Sulphaguanidine has been much used in the treatment of dysentery and with success, but it acts more slowly than the readily-absorbed sulphonamides, such as sulphadiazine and sulphamezathine, and these are therefore preferable in the acute stage.

Sulphapyridine is fairly active and can be used effectively in most systemic infections, but the side effects, such as nausea, vomiting, cyanosis and depression, make it unsuitable for most patients.

Many of the bacterial infections are susceptible to both sulphonamide and penicillin, e.g. infections with the hæmolytic streptococcus, streptococcus viridans, staphylococcus, pneumococcus, meningococcus and gonococcus, and also certain clostridia (*welchii*, septicum and tetani), bacillus anthracis and the actinomyces. In general, it may be said of these that if there is no suppuration, necrosis or bacteræmia, they should be treated by the sulphonamides, but if any one of these is present penicillin is the drug of choice. Even in the absence of such indications, penicillin is preferable in severe illness due to one of these infections, and particularly the following:—cellulitis, mastoiditis, meningitis (except meningococcal), pericarditis, endocarditis, peritonitis, puerperal sepsis, osteomyelitis, suppurative arthritis and infected wounds.

Pneumonia, according to the evidence so far available, is equally benefited by the sulphonamides and penicillin, so that unless the patient is known to be sensitive to the sulphonamides, penicillin will not be required. It should, however, be used in all who fail to respond to a potent sulphonamide within 30 hours. Of the sulphonamides, sulphamezathine or sulphadiazine is generally the drug of choice, and large doses should be used in all except the mildest cases.

Staphylococci are not for the most part very susceptible to the sulphonamides, and some strains are entirely resistant.

In gonococcal infections, the sulphonamides are still used, but are less effective than penicillin.

Meningococcal infections respond very satisfactorily to the sulphonamides.

The coli-typhoid-dysentery group of organisms, the Ducrey's bacillus, bacillus Friedländer, the pasteuræ and brucellæ are not susceptible to penicillin. In these the sulphonamides are still the first choice, though in typhoid and paratyphoid fevers they have, for some unexplained reason, been found inactive. All forms of bacillary dysentery are susceptible, the severe Shiga infection being most affected and the mild Sonne type least.

Urinary infection, whether due to bacterium coli, proteus vulgaris or staphylococcus aureus or albus, responds so much more rapidly to the sulphonamides than to alkalis. It is a wise precaution to re-examine the urine microscopically and by culture a few days after completion of treatment, so that recurrence may be detected and complete investigation, if necessary, carried out. Sulphamezathine gives very satisfactory results and may often be used in much smaller doses than in infections of other systems, but results are more reliable when full doses are used. Mandelic acid therapy requires careful control of urinary pH, and cannot be used in the presence of an impaired renal function; it should be reserved for infections due to the streptococcus faecalis, as this does not respond to the sulphonamides.

The Effect of Procaine on the Inhibitory Factor of Penicillin

By F. P. HESSER

and

M. GOLLAND

(Abstracted from the *Military Surgeon*, Vol. 98, January 1946, p. 47)

MANY complaints have been received from patients of the painful and burning sensation upon intramuscular injections of penicillin. It has been suggested that if

some anæsthetic agent could be used with the administration of penicillin, it would eliminate some of this discomfort to the patient. In this particular procedure, the penicillin solution was prepared by using a 1 per cent sterile procaine solution instead of the usually sterile distilled water or saline. The purpose of this work was to ascertain whether the procaine solution affected the inhibitory factor of the penicillin upon the growth of a particular strain of staphylococci.

The higher concentrations of penicillin dissolved in both distilled water and 1 per cent procaine produce zones of inhibition practically equal in size.

It is concluded that the inhibitory strength of penicillin on the growth of staphylococci is not appreciably altered when 1 per cent procaine is used as the solvent in place of distilled water.

Hepatitis after Penicillin Injections

By LEONARD HOWELLS

and

J. D. OLAV KERB

(Abstracted from the *Lancet*, i, 1946, p. 51)

THE authors have treated 47 patients who had received penicillin injections chiefly for gonorrhœa and syphilis. The average period between injections and onset of icterus was 97 days, with a lower limit of 62 days and a higher limit of 157 days. The degree of jaundice was slight in 13, moderate in 20 and severe in 8 cases; it lasted on an average 21 days. In general, the clinical features were identical with those found in infective hepatitis, and complications were rare. It is thought that penicillin is not the direct cause of the hepatitis, which may be due to some ieterogenic agent, e.g. a virus, transmitted by faulty injection technique, and it seems likely that the cause is analogous to that responsible for late jaundice after antisyphilitic arsenical therapy. It follows that penicillin injections must be carried out with scrupulous care and every precaution taken to avoid transmitting an ieterogenic agent.

The Immunization of Fowls against Mosquito-borne *Plasmodium gallinaceum* by Injections of Serum and of Inactivated Homologous Sporozoites

By P. F. RUSSELL

and

B. N. MOHAN

(Abstracted from the *Journal of Experimental Medicine*, Vol. LXXVI, 1st November, 1942, p. 477)

THIS paper reports attempts to immunize domestic fowls against mosquito-borne infections of *Plasmodium gallinaceum* by means of (a) vaccination with inactivated homologous sporozoites; (b) injections of sera, both normal sheep serum, and serum from fowls chronically infected with the homologous *Plasmodium*; (c) combinations of both sporozoite vaccine and serum.

It was possible to reduce the normal malaria death rate (55.4 per cent) in these fowls by each of the above methods but most markedly by the combined prophylactic treatment. Mortality rates were 21.1 per cent in vaccinated fowls, 16.7 per cent in serum-treated fowls, and 7.3 in those having the combined treatment.

Intensity of infection was measured by counting the percentage of red cells infected each day. It was found that in each group of fowls having prophylactic treatment the average of highest percentages of red cells infected was less than in untreated malarious fowls (30.1 per cent). The average figure was 20.5 per cent in vaccinated fowls, 17.9 per cent in those having serum injections, and 15.0 per cent in those having combined treatment.

The prepatent period was not markedly affected by any of the prophylactic procedures. It averaged 9.1 days in the untreated group, 8.9 days in both the vaccinated and serum-treated groups, and 9.7 days in the group having combined treatment.

The results seemed to demonstrate an interaction of both cellular and humoral agencies in defence against malaria, since the greatest immunizing effect was seen in the series having both sporozoite vaccine and serum injections.

Report of an Attack of Blackwater Fever Subsequent to Induced Malaria

By S. F. KITCHEN

and

G. G. SADLER

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXV, September 1945, p. 379)

THE malarial background and clinical aspects of an attack of blackwater fever have been described; the episode occurred in a white female patient, age 37, subsequent to malaria therapy.

The patient had experienced an infection with one strain of each plasmodial species during the preceding 13 months; *P. vivax* had been allowed to disappear spontaneously, and *P. malariae* had been suppressed by a course of plasmochin; the falciparum infection, in spite of a course of quinine administered following the acute phase of the attack, persisted for five months, with minor parasitic and consequent clinical activity during the latter period of the infection.

Onset of the hæmoglobinuric episode probably occurred within 12 hours of initiation of quinine medication; it was characterized by emesis and the rapid development of icterus; fever, unaccompanied by rigor, appeared about 11 hours after onset.

The attack lasted one week and was featured by: anæmia, involving the loss of 70 to 75 per cent of circulating erythrocytes in the first 24 hours; moderate emesis, chiefly bilious early in the attack; daily fever in the afternoons (continuously at or above 100°F. for 48 hours on the third to fifth days), with rigor on the sixth and seventh days; hæmoglobinæmia, hæmoglobinuria and proteinuria during the first two days; bilirubinæmia (10.2 mg. per cent on the second day) and intense icterus which gradually decreased after the second day; a state of near collapse on the second day; œdema on the fifth to seventh days; the absence of microscopically detectable parasites from the peripheral blood.

Treatment chiefly comprised blood transfusions, infusions of saline and glucose, moderate dosage of alkali by mouth, and supplementary oxygen.

Cardiovascular Disturbances in Tsutsugamushi Disease

By M. SOKOLOV

and

L. H. GARLAND

(Abstracted from the *United States Naval Medical Bulletin*, Vol. XLV, December 1945, p. 1054)

A STUDY of the literature reveals that the typhus group of diseases produces an acute focal and diffuse myocarditis, and frequently during the acute illness, circulatory disturbances occur that may be due either to peripheral or acute myocardial failure. Acute myocarditis has been shown histologically to occur in tsutsugamushi disease as well as in epidemic typhus. The convalescence in many cases of tsutsugamushi disease is protracted, and disabling circulatory symptoms may persist 6 months after the onset of the disease.

Thirty-five patients convalescing from tsutsugamushi disease have been studied; the average interval from the onset of the infection was 4.7 months. The predominant symptoms have been those usually attributed to effort syndrome and vasomotor instability.

Objective evidences of residual impairment of the cardiovascular system were manifested by demonstrable decrease in duration of breath holding, abnormally rapid pulse response to standing and mild exercise, by minor changes in the electrocardiogram, by occasional enlargement of the heart, as demonstrated roentgenographically, and by the presence of 'peaked' waves of myocardial abnormality in the cardiac kymogram.

The pathogenesis of these disturbances is speculative, and whether they are caused by vasomotor instability, residual rickettsial myocarditis, or possibly cerebral medullary lesions is not known.

Militarily the prolonged vasomotor instability in the healthy young men who acquire tsutsugamushi disease is of great importance. They are incapacitated for full military duty for many months, and with the possibility of increased incidence of the disease in future operations, the problem of control becomes of even greater urgency.

Penicillin Alone in Neurosyphilis

By JOHN H. STOKES, M.D.

HOWARD P. STEIGER

and

OTHERS

(Abstracted from the *Journal of the American Medical Association*, Vol. 131, 4th May, 1946, p. 1)

THE Penicillin-Syphilis Group at the University of Pennsylvania has treated 746 patients with penicillin since 11th November, 1943. Of these, 283 had neurosyphilis. The average period of observation is 357 days, the longest period of observation being 719 days. One hundred and nineteen had been observed from 120 to 364 days, 55 for 365 to 599 days and 23 for 600 days and over. Thanks to the follow-up workers of the Institute for the Control of Syphilis, 97.7 per cent of these patients have been kept track of and returned for periodic observation and treatment.

DRUG AND METHODS OF USE

Sodium penicillin from different manufacturers was used throughout. When possible but not invariably, each patient received the product of a single manufacturer.

CONCLUSIONS

1. The effects of penicillin alone in neurosyphilis, in single or repeated courses in a dosage range of 1.2 million to 10 million units and over, were observed.
2. Penicillin sodium in saline solution in a round-the-clock three-hour intramuscular administration technique is effective to greater or less degree in the treatment of all aspects of neurosyphilis studied.
3. An adequate mechanism for spinal fluid examination and testing in *sine qua non* to the work. Effective follow-up was secured in over 97 per cent of our cases.
4. The most striking effects of penicillin are exerted on the spinal fluid formula, the most sensitive and dependable of our indexes.
5. There is no apparent concomitance between spinal fluid response and serologic response in the blood. The spinal fluid responses suggest almost a tropic selectivity of penicillin for the nervous system.
6. There is a steady and definite increase in the proportion of normal and near normal spinal fluids (not mere 'improvement') obtained in our original group of patients under penicillin from 2.6 per cent at the start to 62 per cent after eighteen months' prolongation of observation and appropriate retreatment.

7. Definite improvement in spinal fluid occurred in 74 per cent, and normal and near normal spinal fluids were achieved in 36 per cent of our total series of neurosyphilitic patients without regard to diagnostic category.

8. Dementia paralytica showed 62 per cent definite improvement but no negative fluids. Normal and near normal fluids were, however, obtained in 39 per cent of dementia paralytica and dementia paralytica with tabes combined; 57 per cent of the tabetic, 60 per cent of the asymptomatic neurosyphilitic, 45 per cent of meningovascular cases and 63 per cent of the congenitally neurosyphilitic. Only 6 fluids in the entire series (3.5 per cent) became worse.

9. Overall clinical improvement of some degree occurred in 65 per cent of symptomatic neurosyphilis. 24 per cent improved strikingly, 41 per cent slightly; 9 per cent were worse. Thirty per cent of those with dementia paralytica improved definitely, 31 per cent of the tabetic, 17 per cent of meningovascular patients.

10. As between 1.2 and less than 4.8 million units (low dosage) and 4.8 to 10 million units and over (high dosage), surprisingly little difference in therapeutic effect is observable. There is a slight trend toward superiority in the higher dosage bracket.

11. There is no conspicuous good effect demonstrable from more repetition of courses so far. The striking thing is the prolongation of the good effect of one course. This does not invalidate the statement (paragraph 13) that most of the improvement obtained is in the first 120 days. Further study of this problem is in progress.

12. The good effect of penicillin on the spinal fluid is continued over weeks and months after administration.

13. The maximum effect is usually secured in the first 120 days; but improvement and final normality may follow even an unsatisfactory or atypical early trend.

14. Asymptomatic neurosyphilis conforms best, and dementia paralytica least, to the 120-day rule.

15. Relapse may occur in fluids that have become negative, but relapse to original formula or severity rarely occurs.

16. It is suggested, but not proved, that more definite meningeal reaction (higher cell counts) favours a good penicillin response.

17. The results in primary optic atrophy are as yet inconclusive. Treatment should be begun early with large doses. Charcot joints have not thus far responded to penicillin intramuscularly, but 2 of 5 cases of gastric crises improved. Lightning pains improved, raising the proportion of good symptomatic results in tabes.

18. A comparison between Co-operative Clinical Group results using older methods including chemotherapy and fever, and our penicillin results suggest that, particularly as the observation of penicillin effects lengthens, it will be found to equal or exceed the efficiency of malaria alone or after routine chemotherapy.

19. Penicillin is outranked by malaria as yet in clinical improvement, probably because of the short observation period of penicillin.

20. In asymptomatic neurosyphilis, penicillin ranks far above other methods as a reducer of the spinal fluid to or toward normal.

21. A single course of not less than 4.8 million units in not less than 7.5 days round the clock, using penicillin sodium in saline solution intramuscularly, would seem in our experience to make the best start and often an adequate total therapy for the majority of cases of neurosyphilis. Observation should be carried over at least a year in the absence of convincing evidence of progression before the effects are evaluated and further measures adopted.

22. The results which have been or (are to be) presented in this paper must be interpreted in light of the fact that from June 1943, the date of inception of the study, to the present, commercial penicillin has been a changing mixture of various substances. The

content of 'impurities' has gradually decreased as potency, in terms of units per milligramme, has increased. The relative amounts of the several identified penicillin fractions G, F, X and K have likewise varied from time to time. Those two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different to-day from what it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

Official Statement Concerning Streptomycin

By CHESTER S. KEEFER, M.D.

(Abstracted from the *Journal of American Medical Association*, Vol. 131, 4th May, 1946, p. 31)

THE Committee on Chemotherapeutics and Other Agents of the National Research Council, at the request of the Civilian Production Administration and the Streptomycin Producers Advisory Committee, is supervising an investigation of the clinical usefulness and possible toxicity of streptomycin. The primary interest of the committee in streptomycin is to determine its effectiveness and toxicity in certain infections which are not susceptible to treatment with sulfonamides, penicillin and other therapeutic agents.

Following is a list of the diseases which are under investigation together with a list of those which are not being investigated :—

DISEASES WHICH ARE TO BE INVESTIGATED WITH STREPTOMYCIN UNDER THE COMMITTEE

1. Gram-negative bacillary infections of the genito-urinary tract resistant to the sulfonamides.
2. Gram-negative bacillary infections with bacteræmia.
3. *Hæmophilus influenzae* infections, including meningitis, pneumonia, middle ear disease and laryngo-tracheitis.
4. Friedländer's bacillus (*Klebsiella pneumoniae*) pneumonia.
5. Typhoid.
6. *Salmonella* infections (paratyphoid).
7. Acute brucellosis with bacteræmia.
8. Tularæmia.
9. Bacterial endocarditis due to Gram-negative bacilli.

DISEASES WHICH ARE NOT BEING INVESTIGATED BY THE COMMITTEE AT PRESENT

1. Chronic idiopathic ulcerative colitis.
2. Lupus erythematosus acutus disseminatus.
3. Leukæmia.
4. Cancer.
5. Fever of unknown cause.
6. Rheumatic fever.
7. Rheumatoid arthritis.

TUBERCULOSIS

For the present only those cases of tuberculosis which were already under treatment prior to 1st March, 1946, are being studied. A broader programme for the study of tuberculosis is planned, but it cannot be undertaken at the present time because of inadequate supplies of streptomycin. It is the hope of the Committee on Chemotherapeutics and Other Agents to explore this problem further. The medical profession will be kept informed of developments.

Official Statement on Penicillin in Syphilis

(Abstracted from the *Journal of American Medical Association*, Vol. 131, 4th May, 1946, p. 34)

THE following statement, for release to the press, was prepared jointly on 22nd April by the director of

the U.S. Public Health Service, and the chairman, Syphilis Study Section, National Institute of Health, and was approved by the Committee of Medical Research and the Food and Drug Administration :—

The Syphilis Study Section of the National Institute of Health, U.S. Public Health Service, became aware some months ago of the fact that penicillin as commercially prepared contained not one but several penicillins, known as G, X, F and K. Penicillin K has been shown to be of little or no value in syphilis and in certain other infections because, as compared with other penicillins, it is rapidly destroyed in the body. The relative effectiveness of the other penicillins, G, X and F, has not yet been determined for syphilis or for other infections.

As commercially supplied during recent months the penicillin of some manufacturers, but not of all, has contained substantial though not preponderant amounts of penicillin K. The proportions of K have not been enough to reduce seriously the value of the drug in the treatment of syphilis or in any other infections; and there is no occasion for alarm on the part of physicians who have used it or of patients who have been treated with it. As currently available and employed, penicillin is the best and safest method of treatment of syphilis yet devised. Any patient frightened by newspaper publicity has only to consult his physician or clinic for his usual recheck examination in order to determine his present status.

The situation as to penicillin is a complicated scientific problem under co-operative study both in laboratories and in clinics working under the sponsorship of the National Institute of Health and by industry. Industry has already taken immediate steps to reduce the K content of commercial penicillin and will rapidly apply further scientific information as it becomes available. The public will likewise be informed of important developments as they occur.

Outbreak of Polyneuritis due to Orthotricresyl Phosphate Poisoning

By R. D. HOTSTON

(Abstracted from the *Lancet*, i, 9th February, 1946, p. 207)

ORTHOTRICRESYL phosphate has been recognized as a cause of polyneuritis affecting only the motor system for over 40 years, having been first reported as the agent responsible for the typical syndrome in cases of pulmonary tuberculosis treated with phospho-creosote.

A later outbreak, called 'ginger Jake', occurred in the U.S.A. in 1930, due to the ingestion of adulterated samples of a 'soft' drink known as 'Jamaica ginger'. Smith *et al.* showed this to be due to orthotricresyl phosphate.

The first cases of orthotricresyl phosphate poisoning from use of cooking oils were reported from Natal, where the toxic agent was found in soya bean oil used for salads and cooking. Similar cases of paralysis due to orthotricresyl phosphate have been seen in Germany during the war, where workers have used adulterated fat substitutes for cooking.

In November and December 1945, patients with bilateral foot drop presented themselves to various doctors and consultants in the Merseyside area.

The patients had a lower-motor-neurone paralysis without sensory changes, ranging from complete paralysis of all muscles supplied by the lateral and medial popliteal nerves to mere weakness of the tibialis anticus muscle on both sides. In addition there was usually a weakness of the extensors of the wrist and fingers and of the small muscles of the hand, particularly the adductor pollicis and opponens pollicis. Knee jerks were usually exaggerated, ankle jerks absent, and the plantar responses unobtainable for flexor, and there was no ankle clonus.

Most of the patients gave a history of 'gastritis' or 'gastric flu' in early November, followed in about

ten days by pains in the calves and anterior tibial compartments, accompanied or succeeded in a day or two by increasing weakness of feet, legs, and later hands.

The diagnosis therefore, by exclusion, came down to one of acute infective polyneuritis.

Triorthocresyl phosphate was among the agents suspected as the cause and has been found in a cotton-seed oil obtained from a single source by all the patients and used as a cooking oil. This compound is used in the manufacture of cellulose, lacquers, varnishes, etc., and it is probable that contamination took place from use of second-hand containers.

Chemotherapy of Pneumococcal Meningitis

By H. V. SMITH *et al.*

(Abstracted from the *Lancet*, *i*, 9th February, 1946, p. 185)

As soon as a diagnosis of meningitis is made, lumbar puncture is performed; a gram-stained film of the cerebrospinal fluid is examined for organisms, and cultures are put up with *para*-amino-benzoic acid. Once pneumococci are seen—and often the fluid is swarming with them—a lumbar injection of 8,000 to 16,000 units of penicillin (2,000 μ /c.cm.) is given, with a smaller range for infants. Systemic penicillin treatment is begun either by intermittent 3-hourly injections or a continuous intramuscular drip, and 120,000 units given in 24 hours. In this dose no appreciable amount penetrates the theca; it is given to control the primary infection, and the septicaemia which may complicate the meningitis. Sulphadiazine is given by mouth or nasal tube in doses of 2 g. every 4 hours, following an initial dose of 4 g., with the usual precautions against renal block.

Within 18 hours—usually 12—another lumbar injection of penicillin is given. The cerebrospinal fluid should by now be sterile and the film show a dramatic decrease in the number of organisms. The fact that the cell content of the fluid has usually increased is not in itself disquieting, but if the fluid is perceptibly thicker than on the previous occasion it is probably wise to do the third puncture 12 hours later, to make sure of detecting any incipient block requiring ventricular injections. Thereafter daily injections are usually sufficient, but even in the mildest cases these must be continued for at least 5 days, otherwise the meningitis may relapse. After 4 to 5 days intramuscular penicillin can be stopped, and sulphadiazine cut down to 1 g. 4 hourly; this dose should be maintained for a week in order to cover the period of withdrawal of the intrathecal penicillin. The first 24 to 36 hours should always be regarded as a period of great anxiety and one in which the general nursing care and the maintenance of a good fluid intake may make the difference between failure and success.

Delay in instituting treatment is usually due to delay in diagnosis. The onset may be fulminating, acute, or insidious.

The type with an acute onset is the commonest.

The case may be one of meningococcal, pneumococcal, or streptococcal meningitis, or the infection may be tuberculous or due to *T. influenzae*. In any case, from the practical point of view it is imperative that treatment with full doses of sulphonamides should be begun immediately. We emphasize the words 'full doses', because too often we have seen that sulphonamide chemotherapy has been half-hearted. The best sulphonamide for meningeal infection at present available is sulphadiazine, but if this be not to hand it is better to begin treatment immediately with sulphamezathine, sulphapyridine, sulphathiazole, or sulphamylamide, in that order of preference, rather than to delay until sulphadiazine has been obtained.

Should penicillin be given intrathecally at the first tap before the lumbar puncture needle is withdrawn? By no means in every case. In meningococcal meningitis it is usually unnecessary; in streptococcal menin-

gitis it may be dangerous; and in all cases, especially in a private house, it carries some risk of secondary infection by introducing penicillin-resistant organisms. Even in pneumococcal meningitis immediate intrathecal treatment is required only by the very severe case.

Where bacteriological facilities are not available the differential diagnosis must be attempted on clinical grounds. There is a useful point of differentiation between pneumococcal meningitis and the commoner meningococcal variety. In at least 4 out of every 5 cases of pneumococcal meningitis a primary focus of infection can be detected, e.g. otitis media, sinusitis, pneumonia, etc., the signs and symptoms of the primary infection are often mild.

If it is to be effective penicillin must circulate freely throughout the subarachnoid space and the whole ventricular system, but this may not always be easy from blockage of cerebrospinal pathways.

In any case, penicillin should be suitable for intrathecal use. Some preparations are intensely irritating and capable in themselves of causing a brisk sterile meningitis. All our recent work has been done with Pfizer penicillin (approximately 500 to 700 units per mg.). The importance of strict asepsis is paramount.

The most important factor in prognosis is delay in instituting effective treatment, for if the infection has been allowed to progress beyond a certain stage all treatment becomes useless. The time when this irreversible state is reached depends on the severity of the infection and in fulminating cases is a few hours only.

Relapses which are unfortunately common, differ in no essential particular from the initial attack. The prognosis is good if promptly recognized and energetically treated.

Treatment of Macrocytic Anæmia with Folic Acid

By T. D. SPIES

(Abstracted from the *Lancet*, *i*, 16th February, 1946, p. 225)

In August 1945, the synthesis of folic acid (*L. casei* factor) was announced by sixteen investigators. The following month Spies, Vilter, Koch and Caldwell reported the results of the first clinical use of synthetic folic acid in the treatment of macrocytic anæmia. They showed that its administration, either by mouth or parenterally, was followed by a striking hæmopoietic response in 9 cases of macrocytic anæmia, a response similar to that which follows the administration of a potent liver extract. These results were quickly confirmed in a larger series of cases reported in December 1945, by Vilter, Spies and Koch. At the same time Spies, López, Menéndez, Minnich, and Koch reported that the macrocytic anæmia of tropical sprue found in Cuba responds in a similar manner. These results marked a milestone in the progress of studies on anæmia which, with the assistance of many associates and collaborators, I have been carrying on for fifteen years.

The present report, which is a tentative evaluation of the status of folic acid as a therapeutic agent in anæmia, is based on the observations made in 45 cases in Birmingham, Alabama, and in Havana, Cuba, and summarizes our findings up to the present time.

In the selection of cases the following rigid criteria were adopted: (1) The patient must have a macrocytic anæmia with red cell counts of 2.5 million or less and a colour index over 1. (2) He must be untreated, or he must not have been treated recently enough to interfere in any way with our evaluation of the effect of folic acid. (3) He must not have any complicating disease which might be lethal during the course of the study. (4) The bone-marrow must contain megaloblasts and have the typical erythroblastic arrest seen in macrocytic anæmia. A fifth criterion used for the selection of any patient in Cuba, where we were studying sprue, was that he must have 'fatty stools' and weight loss.

The diagnosis in these cases was only made after intensive study by a number of physicians. Of the 45 patients, 41 had typical macrocytic hyperchromic anaemia diagnosed on the basis of criteria used in the past in the Nutrition Clinic in Birmingham, Alabama. The other 4 patients had iron-deficiency anaemia characterized by a low colour index.

All the patients except 4 were admitted to hospital for preliminary observations, base-line determinations, and therapy. These 4 patients, who lived near the Nutrition Clinic in Birmingham, were treated as ambulatory cases. They came to the clinic daily throughout the period of study.

Throughout the time they were in the hospital, the diet of 35 of 41 in-patients was rigidly controlled. Meat, meat products, fish, and poultry were omitted, and only a quart of milk and one egg daily were allowed. Bread, cereals, sugar, fats, vegetables, and fruits were permitted in any amount desired. A similar diet had been used in 75 cases of anaemia studied previously, and no hæmopoietic response had occurred in any of these patients while they were on this diet. We felt reasonably sure, therefore, that any hæmopoietic response would be from the folic acid administered rather than from any food the patient received.

Synthetic folic acid was administered either parenterally or by mouth. Two patients received 20 mg. and 4 received 50 mg. intravenously every day; 2 patients received 20 mg. intramuscularly every day. To get the folic acid into solution for injection we converted it into a soluble salt by adding normal sodium bicarbonate solution. To ensure sterility the solution was then passed through a Seitz filter. To the remaining 34 patients the folic acid was given by mouth. Five patients (3 with pernicious anaemia and 2 with nutritional macrocytic anaemia) were given 10 mg. or less. The other 29 patients were given daily doses ranging from over 10 mg. up to 400 mg. When the dose was 20 mg. or more, half of it was given in the morning and the other half in the afternoon. For oral administration it was prepared by mixing it to a smooth paste with four or five drops of cold water and stirring it constantly while enough water was added to make 20 c.cm. After the patient had taken this mixture, water was added to his glass to rinse it well; and the patient also drank this in order to ensure his getting all the folic acid.

RESULTS

The following 26 cases responded to folic acid therapy: 5 patients with nutritional macrocytic anaemia, 5 with Addisonian pernicious anaemia, 8 with sprue, 3 classed as indeterminate, 3 with macrocytic anaemia of pregnancy, 1 with macrocytic anaemia associated with chronic alcoholic addiction, cirrhosis of the liver and neuritis, and 1 with macrocytic anaemia associated with carcinoma of the stomach. In these 26 cases the initial red cell count ranged from 1.1 to 2.97 million and averaged 1.87 million; on the fourteenth day it ranged from 1.58 to 3.57 million and averaged 2.69 million. The initial hæmoglobin ranged from 5.9 to 9.9 g. and averaged 7.68 g.; on the fourteenth day it ranged from 7.1 to 11.7 g. and averaged 9.73 g. The first day of reticulocyte rise occurred from the third to the seventh day; the peak occurred on the third to the eighth day. The reticulocyte count at the peak ranged from 4.6 per cent to 31.8 per cent and averaged 17.2 per cent.

SUMMARY AND CONCLUSIONS

These findings show that the administration of synthetic folic acid, either by mouth or parenterally, is followed by a prompt hæmopoietic response in persons with Addisonian pernicious anaemia, nutritional macrocytic anaemia, the macrocytic anaemia of pregnancy, pellagra, and the macrocytic anaemia of the sprue. Associated with this hæmopoietic response is a striking increase in strength, vigour and appetite. The subjective and objective improvement is similar to that which follows therapy with potent liver extract. Folic

acid was not found to be effective in iron-deficiency anaemia, aplastic anaemia or leukaemia.

Determination of the minimal and average dose of folic acid will require the study of many cases. Our findings up to the present indicate that there is some variation in individual requirements. We have given as much as 400 mg. by mouth without ill effects, and we have had five patients who have responded to 10 mg. administered by mouth. Previously, one of these patients had failed to respond to 3 mg., one to 4 mg., and three to 5 mg. of folic acid administered by mouth daily for ten days. We tentatively suggest a total dosage of 20 mg. parenterally or 20 mg. by mouth.

A restricted diet was given to some patients in order to determine the anti-anaemic properties of folic acid as accurately as possible. We wish to stress that neither folic acid nor any other single chemical substance can be expected to take the place of all the nutrients essential for good nutrition. We do not recommend a restricted diet in the treatment of macrocytic anaemia—in fact, we prescribe a diet high in protein, minerals, and vitamins.

Despite the fact that there are no published reports by other workers confirming our findings, our results are so striking that I have no hesitation in saying that folic acid, a vitamin present in liver, yeast, and other food materials, is a potent anti-anaemic factor in persons with certain types of macrocytic anaemia in relapse.

Gonadotropins in Urine of Aged Eunuchs

(Abstracted from the *Indian Medical Record*, Vol. 66, May 1946, p. 132)

J. B. HAMILTON *et al.* (*Journ. Clin. Endocrinol.*, May-June 1945, 5, 203) made a study of titres of urinary gonadotropins excreted by four ageing men who had been eunuchs from 8 to 12 years of age and who, at the time of study, had been eunuchs from 44 to 51 years, and compared the figures with those of 10 normal old men aged 55 to 76 years. The average daily amount in M.U. were respectively 160, 160, 40 and 40 to 80 as against 10 to 25 by normal men. These supranormal titres are comparable to those generally found subsequently to the castration of mature men. As the quantity of urinary gonadotropins of all the normal old men studied was within the range reported for normal young men it is concluded that climacteric conditions comparable to those in women do not appear to be the normal sequelæ of ageing in men although primary gonadal insufficiency does occur in old men after bilateral orchietomy or destruction of the testes.

This excess of urinary gonadotropins over normal figures is characteristic of castrate men regardless of whether (1) orchietomy is carried out before or after puberty, or (2) the period of time after castration is brief or prolonged.

A. B. R. C.

Rubella

(Abstracted from the *Medical Officer*, Vol. 75, No. 20, 18th May, 1946, p. 191)

LONG and Danielson have reported, as quoted in *American Medical Newsletter* (September 1945), that cataract with microphthalmos in the babies born of mothers who suffered from rubella at 2 to 6 weeks of gestation is due to the result of intrauterine damage by rubella.

Though the conclusion cannot be accepted without much more evidence it is to be noted that the apparently trivial virus diseases may be responsible for more damage than is usually ascribed to them. Moreover, anything bearing on the causes of congenital malformations from arrest in development due to some disease process acting at an early date of

pregnancy is welcome as most of these cases are not hereditary.

A. B. R. C.

[For rubella in the mother being responsible for deafness in the baby see this journal, vol. 81, p. 315.—Editor, *I.M.G.*]

Animal Disease Communicable to Man

(Abstracted from the *Medical Officer*, Vol. 75, No. 21, 25th May, 1946, p. 199)

ANIMALS may be an ætiological factor in human disease in four ways: (1) infections which are primarily of animal origin, (2) infections in which the causal organism is primarily a human pathogen, (3) infections in which the rôle of the bovine is that of a passive carrier, (4) infections by parasites which pass one stage of their existence in man and another in an animal other than man.

Very few pathogens are common to man and any other animal. Pathogens that are primarily parasitic upon animals may invade a human host and set up disease, but they do not spread from one human to another. This is partly due to the means adopted to prevent them from doing so.

Psittacosis is due to a virus symbiotic with many birds. The virus, if harboured by man, does nothing serious at present, but it is possible that it might become attuned to man with serious consequences.

Pasteurella is a parasite of rodents communicable to man by the bites of rat fleas. Occasionally pasteurella undergoes some modification in man giving rise to epidemics of the fatal pneumonic plague which is intensely infectious from man to man. These epidemics die out completely for reasons not known to us.

Tuberculosis attacks all vertebrates, but is rare except in man and domesticated cattle, pigs and poultry. The extent, if any, to which man is infected by pig tuberculosis is unknown. Cattle tuberculosis is very frequent in man, but so far we have been unable to find out if bovine tuberculosis is infectious from man to man.

As man is a recent product of evolution, it is not improbable that many of his parasites were originally of other animal origin, but most which trouble us to-day are now exclusive to our species. No other animal now suffers from natural diphtheria, but many can be given the disease artificially. Some varieties of *Salmonella* are parasitic both to other mammals and man while paratyphoid is parasitic only to man.

There have been many theories to explain the behaviour several of which presume some alterations of body chemistry some of which changes encourage and others inhibit the growth of non-nucleated organisms within us and possibly changing their nature. Something of this kind is the basis of chemotherapy.

A. B. R. C.

Treatment of Subacute Bacterial Endocarditis with Penicillin

Report of 10 Cases

By L. H. SIGLER, M.D.

T. J. LONGO, M.D.

and

H. H. FELDMAN, M.D.

(Abstracted from the *New York State Journal of Medicine*, Vol. 46, No. 6, 15th March, 1946, p. 625)

TEN patients with subacute bacterial endocarditis were treated with penicillin. Four of these are living and well, two, nine, twelve, and fourteen months, respectively, after therapy was discontinued. One patient died from a cerebral embolus after all signs of

the disease subsided, and autopsy revealed healed verrucae on the mitral valve. Two patients died from congestive heart failure after all signs of subacute bacterial endocarditis had subsided. One patient died because an insufficient amount of penicillin was given and another because of other complicating diseases. Only one patient, presumably effectively treated, died from subacute bacterial endocarditis itself.

The simplest and efficient method of administration of penicillin in subacute bacterial endocarditis is by the intramuscular route in doses of not less than 25,000 units every two hours for three to six weeks. There is no definite advantage in the intravenous route, although it should be used if the response by the intramuscular is not satisfactory. There is no advantage in the use of heparin in combination with penicillin, and it carries considerable hazard.

A. B. R. C.

An Effective Control Programme for Rabies

By ROBERT H. BROAD, M.D.

and

ALEXANDER ZEISSIG, D.T.M.

(Abstracted from the *New York State Journal of Medicine*, Vol. 46, No. 2, 15th January, 1946, p. 167)

A CONTROL programme for rabies that worked out effectively in the case of Tompkins country is outlined.

As a pre-outbreak activity night quarantine was imposed on dogs of places where the animals were in great numbers, i.e. of the Department of Agriculture and Markets, dog wardens were authorized to dispose of all unwanted stray dogs, and the public were kept alert of the disease and made to report all dog bites. A plan to be enforced in future outbreaks was also prepared consisting of (i) unification of control by pooling the resources of different groups, (ii) advisory council with both official and non-official personnel, (iii) public education and public relation through press, radio, posters, etc., as regards the importance of early treatment and identification of dogs by short precise and properly spaced articles, (iv) quarantine, preferably at the public expense, 7 days for rabid dogs and 4 months (or alternatively destruction) for dogs bitten by rabid dogs, extending to the surrounding area, violates being first warned and later fined, and isolation for healthy dogs, and (v) vaccination of all dogs free or at a minimum expense accompanied by necessary instructions.

A. B. R. C.

Two Causes of Pain in the Right Iliac Fossa

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 2nd March, 1946, p. 303)

DETERMINATION of the cause of a pain on the right side of the lower part of the abdomen is an important and often not an easy matter. There have recently appeared discussions of two conditions which cause such pain, but which perhaps are not thought of often enough. Ian Aird describes acute non-specific mesenteric lymphadenitis and James A. Greene writes of the syndrome of psoas myositis and fibrositis.

The glands most often affected are the juxta-intestinal group of the mesenteric glands, lying along the mesenteric attachment of the lowest few feet of the ileum. Later the intermediate and terminal mesenteric glands along the ileal arteries and on the main superior mesenteric trunk become involved. Sometimes the cæcal and ileo-colic groups of glands are similarly affected. The patients are usually children beyond the age of infancy. The outstanding symptom is severe colicky abdominal pain, most intensely felt in the lower part of the abdomen on the right side, but not precisely localized by the patient. Nausea and vomiting may occur. Recurrent attacks are common. The temperature is often of the order of 101°F., and there

is a neutrophile leucocytosis. The abdominal tenderness is higher and more medial than is usually in appendicitis, and the site of maximum tenderness often shifts to the left, perhaps even beyond the mid-line, if the patient turns from the supine to the left lateral position. The overlying muscles have increased tone, but relax under steady pressure. The enlarged glands can seldom be palpated. There is sometimes evidence of a recent or accompanying upper respiratory tract infection.

Acute appendicitis is the condition most likely to be confused with acute mesenteric adenitis. We agree with Aird that distinction is usually possible, but most clinicians have been accustomed, in making a distinction, to emphasize the disproportionate temperature and the frequent presence of a throat infection rather than the abdominal signs. Aird writes: 'The sharp spasms of colic with complete or almost complete freedom from pain between them, the rolling and kicking of the child in an attack, the high and medial situation of the tenderness, the absence (if it is absent) of rebound tenderness even at the point of maximum tenderness, the presence (if it is present) of shifting tenderness, the relaxation under steady pressure of apparently rigid muscles, the history of previous typical recurrent attacks if these have occurred, all inspire confidence in a negative diagnosis of "this is not appendicitis"'. It is true that this clinical picture is more suggestive of mesenteric adenitis than of appendicitis, but acute appendicitis in the child, particularly the young child, is often an atypical and treacherous complaint, and it is a comfort that there is usually further evidence that helps to exclude it. One very valuable further sign is the temperature. Appendicitis does not cause a high temperature until it advances to peritonitis, at least local, or abscess formation. Mesenteric adenitis usually does. If the temperature is above 100°F. and it is not apparent that inflammation has spread beyond the appendix, then appendicitis will rarely be the underlying illness. The

obscurity of an inflamed appendix lying in the pelvis, of course, must not be forgotten. An equally valuable fact in our experience is that mesenteric adenitis is very often, indeed we think usually, accompanied or preceded by an acute upper respiratory infection, a reddened nasopharynx with often some post-nasal mucopurulent discharge. Aird admits that this is a 'not unusual concomitant of non-specific mesenteric adenitis, but neither its presence nor its absence is highly significant, for in more than 70 per cent of my cases pharyngitis has not been detected, and acute pharyngitis sometimes closely precedes acute appendicitis'. We should have been inclined rather to the view of Olney and Adams, quoted by Aird, who regarded mesenteric adenitis as 'a local manifestation of a generalized condition from upper respiratory tract infection'. A confident diagnosis of acute mesenteric adenitis can often be made, but if after consideration of all these factors appendicitis cannot be excluded with assurance, then in the interests of safety operation may well be the right course.

Psoas myositis and fibrositis, described by Greene, may cause pain in either or both lower quadrants of the abdomen. It may persist for days or for even as long as years. It is increased by activity that involves use of the ilio-psoas muscles, and is revealed by tenderness along these muscles and pain on contracting or stretching them. Diagnosis is usually easy enough if the condition is kept in mind. Irritation of the psoas may, of course, result from inflammation of organs adjacent to it, particularly the appendix and urinary tract, but occasionally the spine, bowel or the female pelvic organs. Disease of these structures must be excluded before a simple myositis or fibrositis is accepted as the cause of the pain. Many incorrect diagnoses were made and ineffective treatments given before the condition was recognized in the patients reported by Greene, errors that in most cases would not have occurred had the physician thought of myositis.

Reviews

PERIPHERAL NERVE INJURIES: PRINCIPLES OF DIAGNOSIS.—By W. Haymaker, Major, M.C., A.U.S., and B. Woodhall, Lt.-Col., M.C., A.U.S. 1945. W. B. Saunders Company, Philadelphia and London. Pp. xiv plus 227, with 225 illustrations. Price, 22s. 6d.

BEFORE being called upon to review this book I had actually used it in dealing with Peripheral Nerve Injuries during the last 5 months, and on the whole found it a useful guide to the examination of cases as well as a good presentation of the material from the point of view of training medical officers.

Like all books it has its faults but I think that many of these are minor and considering that it is a book produced under service conditions the authors are to be congratulated.

Perhaps the anatomical data might have been collected together as one part rather than presented as now diffused through the text with much repetition. On the other hand repetition has its advantages and it is convenient to have things repeated rather than to have to turn back to one part continually. A more distinct division might have been made between early and late injury results, since these are two distinct clinical types and search for the data is a little tedious. More information on the detailed study of primary and secondary movers would have been of value. Supplementary and trick movements, the detection of which is so important and requires such close analysis, are not described at all, and the sensory examination is almost completely neglected.

Some of the photos and charts of sensory derangements are incomplete or do not indicate the data available. Apart from these major points there are

one or two minor points which doubtless the authors will correct for themselves the moment they see them in print; one which does require mention is the confused definition of chronaxie; the paragraph on page 76 dealing with this is not clear and requires a complete revision.

The publishers are to be congratulated on the get-up of the book, the quality of the paper and the reproductions. As a war-time production it is magnificent.

A. T. A.

MODERN ANÆSTHETIC PRACTICE.—Edited by the late Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., F.R.C.P., and Alan Moncrieff, M.D., F.R.C.P. Second Edition. 1946. Published on behalf of the 'Practitioner', 5, Bentinck Street, W.1, by Messrs. Eyre and Spottiswoode (Publishers) Limited, London. Pp. viii plus 150. Illustrated. Price, 12s. 6d.

ON first sight this appears to be a small practical book for the practitioner doing anaesthetics in addition to general practice. On looking into it more closely the object does not appear so clearly for although to a practitioner well versed in anaesthetics the articles present him with a cursory review of present anaesthetic practice, to the less expert, some of the chapters will be disappointing for they do not give more than a sketchy review. A busy practitioner would like such a small volume to contain technical information of proved value such as he may refer to quickly in his car, on the way to hospital or nursing home.

Like all symposiums the differences in style of each of the authors create a sensation of differences of

quality which may be deceptive, and do injustice to one whilst overrating another.

Dr. Blomfield's introduction is good, and his analysis of the present situation of anaesthetic practice is clear and brief. The first four chapters contain reviews of the theory of anaesthesia, use of volatile anaesthetics, nitrous oxide and basal narcotics. The first two chapters are excellent but lack references to guide the interested, but little experienced, practitioner in a choice of profitable reading for the limited time he may have available.

In chapter III, Professor MacIntosh gives a precise and a practical survey of nitrous oxide administration, but again without references.

Brigadier Ashworth, in chapter IV, supplies some useful references which enhance the value of his chapter and make it possible to use it as a guide for a House Surgeon. He gives details of technique which are clear and easy to follow.

Chapter V would have been improved by the use of a few line drawings and diagrams, in economy of much reading.

Authors in England should remember that long descriptions in English are difficult to follow by the people of countries where English is merely the language of examinations. Line drawings explain far more to these people, as they do also to anyone else, apart from saving time and leaving deeper memory impressions.

It is a pity Dr. Hasler has not given us a more practical chapter on spinal anaesthesia; he certainly explains some points of difficulty but, as one who gives his own spinal anaesthetics, I would have appreciated a clear description of his preferred technique, with its variations and his treatment of the complications. Again he gives no references.

Chapters VII and VIII are excellent.

Chapter IX is good but would be more valuable if details of technique, such as spheno-maxillary block, had been given. Again no references.

Chapter X, in the same way, lacks short exact descriptions of techniques for the common regional blocks. The use of amethocaine which gives such prolonged and even anaesthesia, and which has recently become popular is not mentioned.

Chapter XI could have been longer and more detailed, for the practitioners' troubles truly begin with the post-operative period and the gathering of anxious relatives at the bedside.

Chapter XII gives a short survey of Anaesthetic Explosions but no reference to recent work on the subject.

This is a disappointing book in many ways, but should be read, with discretion, by all practitioners interested in anaesthetics and by all junior anaesthetists.

A. T. A.

THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE.—By C. H. Best, C.B.E., F.R.S., and N. B. Taylor, F.R.S., F.R.C.S. Fourth Edition. 1945. Baillière, Tindall and Cox, London. Pp. xiv plus 1169, with 497 illustrations. Price, 55s.

THE labour spent on writing a comprehensive account of close correlations between the latest developments in physiology and medicine is enormous. Further, the need for revising such an account is twice as great as it would be in either of the two subjects singly. The present book is the result of a successful attempt at the correlation and revision. A progressive physician must have access to it.

The basic physiological items are treated with conciseness and precision in 9 sections and 81 chapters. The new two-column format helps both the reader (by bringing a whole paragraph before the eye at a time) and the printer (by reducing the length of the line in which a correction is to be made).

In the next edition the table on blood groups on page 37 may be readjusted and the linkage between the laboratory and the clinic made more complete in the matter of the intrapleural pressure which the physiologists measure in mercury and clinicians in

water: the book appears to measure it in mercury only.

In conformity with the economy standard the get-up is satisfactory. A few printer's errors (one occurs on page 297, last but one line, 'n' instead of 'in') are not likely to cause inconvenience.

S. D. S. G.

HOWELL'S TEXTBOOK OF PHYSIOLOGY.—Edited by John F. Fulton, M.D. Fifteenth Edition. 1946. W. B. Saunders Company, Limited, London and Philadelphia. Pp. xxxv plus 1304. Illustrated. Price, 40s.

THIS well-known textbook of physiology has been thoroughly revised by a team of editors and other contributing authorities collaborating with Professor Fulton, in all numbering 24.

While the fluent prose style of the original has been preserved newer developments have been presented *de novo* rather than worked into the older text. Some sections on old topics have been rewritten completely. The physiological studies of sex and aviation include the latest developments in these rapidly unfolding items of knowledge.

Perhaps the sections on nervous system which take up nearly half of the book could have been reduced to provide space for endocrinology which is still treated along old lines. The alleged features in an old picture of a decerebrated cat (hyperextension of the neck, opisthotonos and extension of the tail, on page 187) are not very striking.

The book is fully representative of modern American physiology and will provide reliable reference to post-graduate workers anywhere. Undergraduates particularly interested in the subject and physicians who keep abreast with the times will find it helpful.

The printing and illustrations, nearly all in black and white, are excellent. No printer's errors attract attention. The paper and binding are decidedly better than those of most standard books produced under economy standards.

S. D. S. G.

THE CHEMICAL COMPOSITION OF FOODS.—By R. A. McCance and E. M. Widdowson. Second Edition. 1946. Published by His Majesty's Stationery Office, London. Price, 6s. net

THE problem of human nutrition as well as the nutritional and dietetic treatment of disease requires, as an essential, an exact knowledge of the chemical composition of food. The Medical Research Council in England has for many years past been collecting data of the analytical work of food chemistry done in that country to provide a standard work on the subject. With this object in view an intensive work on the analysis of foodstuff was started by McCance and others at the King's College Hospital, London, in 1925, and more recently at the Department of Medicine, Cambridge.

Comments are unnecessary on the present volume which comprises mostly of a reliable collection of data published from time to time. The authors, who were themselves the pioneer workers, have taken trouble to scrutinize the whole work and make corrections wherever there were doubts about the validity of the figures after subjecting them to fresh analysis.

The figures as given in the book can thus be taken as true and correct and herein lies the great value of the book as a standard book of reference in the matter of chemical composition of foods.

J. P. B.

FORENSIC CHEMISTRY AND SCIENTIFIC CRIMINAL INVESTIGATION.—By A. Lucas, O.B.E., F.R.I.C. Fourth Edition. 1945. Edward Arnold and Company, London. Pp. 340. Price, 25s.

In the present, fourth, edition of this book the general plan of the last edition has been preserved although alterations and additions have been made throughout.

Forensic matters dealt with are many and go beyond the range of forensic medicine. Naturally all of them have not been treated in detail. References and bibliographies, however, are ample and put the seeker on the path every time.

Some lack of agreement may exist on the following : (1) The test of blood by antisera (p. 23). This is an immunological, not a biochemical reaction. The worker should be able to make his own antisera. (2) The light used in searching for stains on fabric (p. 24). Candle light falling obliquely is useful and easily available. (3) Dyes (p. 37). They do show a spectrum which may be mistaken for that of (cyan) hæmochromogen (Grevil, S. D. S., Chowdhury, A. B. R., and Das, B. C., *Indian Journ. Med. Res.*, **33**, 173, 1945). (4) Stains not giving the benzidine test (p. 37). They are best rejected: further examination including spectroscopy is not necessary. (5) Differentiation between bloods of sheep and goat or other closely related species (p. 38). This is possible with complement fixation tests. (6) The adsorption (=absorption) method in precipitin test (p. 38). This is not a success. Further, it is the *ring* not the *turbidity* which should be aimed at. (7) Incubating bloodstains (p. 39). At least in the tropics prolonged soaking at blood heat leads to trouble. Half an hour or so at room temperature is ample. Prolonged soaking at ice box temperature may at times be necessary to get the solvent into joints of weapons. (8) The salicyl-sulphonic acid test (p. 41). The 'upwards' figure indicative of the dilution must be limited. (9) The method of determining blood groups (p. 47). The use of whole blood is undesirable and the testing serum from group B (serum α or better still serum α) might as well be on the left side of the slide to detect group A on that side.

The length of the last paragraph (which could be made longer) is directly proportional to the readability of the book which has become one of forensic classics in laboratory methods. No one entrusted with criminal investigation, inside or outside a laboratory, can afford to do without it, particularly in the matter of Documents and Firearms, etc., which together form more than one-third of the book.

The author's methods of scientific criminal investigation in Egypt are applicable in India.

The get-up has been markedly affected by the 'authorised economy standards'. It is hoped a reprint (minus the errata) on better paper and better bound will soon be available. The small type, unfortunately, will remain until the next edition.

S. D. S. G.

TEXTBOOK OF MEDICAL TREATMENT.—Edited by D. M. Dunlop, B.A. (Oxon.), M.D., F.R.C.P. (Edin.), M.R.C.P. (Lond.), L. S. P. Davidson, B.A. (Camb.), M.D., F.R.C.P. (Edin.), F.R.C.P. (Lond.), and J. W. McNea, D.S.O., D.Sc., M.D. (Glas.), F.R.C.P. (Edin.), F.R.C.P. (Lond.). Fourth Edition. 1946. E. and S. Livingstone Limited, Edinburgh. Pp. xix plus 923. Price, 30s.

LITTLE need be said about the new edition of this well-known book by the distinguished Scottish writers. The passage of a textbook through four editions with two reprints over a period of less than seven years is sufficient evidence of its success. In this edition, the format has been changed, and the book has become larger but slimmer. Among the additions we notice that a new chapter has been added on penicillin therapy, the sections on venereal diseases and diseases of the thyroid gland have been rewritten, and the chapter on respiratory diseases has been revised while a short account of D.D.T. has been included in a postscript to the book. We have, however, a few criticisms to make. Thymol has been given the first place as an anthelmintic in the treatment of ancylostomiasis, but very few would really recommend its use now. Although excellent results of the treatment of bacillary dysentery with sulphonamides have been mentioned, it gives us a shock to read in 1946 'An initial dose of $\frac{1}{2}$ ounce of castor oil . . . followed by

the administration of 1 drachm of sodium sulphate every two hours . . . is a routine method of treatment'. Anthiomalin tops the list of drugs recommended for treatment of kala-azar, but is hardly used in practice. Penicillin has not been mentioned in the treatment of agranulocytosis. We hope these will receive due consideration at the next revision, while the present one will maintain the popularity of the previous editions.

R. N. C.

AN INTRODUCTION TO MEDICAL SCIENCE.—By William Boyd, M.D., F.R.C.P., F.R.S.C. Third Edition. 1945. Henry Kimpton, London. Pp. 366 with 125 engravings and a coloured plate. Price, 18s.

THIS book, designed for nurses, is meant to give an 'airplane view' of disease, its causes and the bodily changes which accompany it, so that they may get a better understanding of their work. The first section of the book deals with the general principles of disease, the second with the diseased organs, and the third with some practical applications. There is a brief summary of the structure and function of each organ, and the symptoms have been described in their relation to the pathological changes. In this edition, a considerable number of changes have been made, including a chapter on the principles of treatment. The book is an introduction to the study of disease, though a sketchy one, but rather too much emphasis has been put on pathology, the details of which may be too much for the nurses who have already got enough to learn. Is it necessary, for instance, for them to know of the mitotic figures of cancer cells, microscopic differentiation between epidermoid carcinoma and adenocarcinoma, or the histopathology of the tuberculous lung? One or two slips under treatment should be mentioned: it is misleading to say that for malaria, quinine must be given for several months, and in view of what mepracine has done for the last war it seems unfair not to mention it. In treatment of amoebic dysentery emetine is not usually given in the form of ipecacuanha. These are, however, small blemishes in an otherwise good introductory book.

R. N. C.

VENEREAL DISEASES IN GENERAL PRACTICE.—By Svend Lomholt, M.D. (Copenhagen), M.D. (Honorary), Riga, O.B.E. 1946. H. K. Lewis and Company, Limited, London. Pp. 231. 39 illustrations in colour in 16 plates and 78 illustrations in black and white. Price, 25s.

THIS work is the first English edition of Dr. Lomholt's book, a Danish textbook which has been used widely in the Scandinavian countries (3rd edition, 1945).

In spite of the small size of the book every item covered by the title has received full consideration in diagnosis and treatment. Pictures, in black and white as well as in colour, are excellent.

Those who have seen English and American works on venereology growing at each edition will find in this book of moderate size a pleasant change. Nothing one sees in a venereal clinic is missed. In the diagnosis and treatment the essential has been presented without interference from the non-essential. Quaint expressions include 'utensils' for douche can, etc.: as a matter of fact douche can, etc., are utensils.

The nomenclature is not strictly in accordance with the English usage. The same is true of most American books. Granuloma Venereum, for instance, has been called Granuloma Venereum Inguinal (which causes confusion with Lymphogranuloma Inguinale). There is no ambiguity, however, in the description and identity of a disease. A supplement gives full information on the use of penicillin, mapharside, etc.

Printer's errors are many, yet they do not lessen the value of the book and are bound to be removed in the next edition. Page 134 is particularly defective in this respect. The index could be made more useful. The binding is indicative of the general want of material in Europe.

All interested in venereal diseases will do well to obtain a copy of this book.

S. D. S. G.

BOOKS RECEIVED

A Note on Food Yeast. By S. R. Sen Gupta. 1946. Published by the Nutrition Committee, Sanitary Board, Government of Bengal, Calcutta.

Problems of Nutrition in Public Health in India (Extracts from the Report of the Health Survey and Development Committee, Government of India, 1946). Compiled by S. R. Sen Gupta. 1946. Published by the Nutrition Committee, Sanitary Board, Government of Bengal, Calcutta.

Lewis's 1844-1944: A Brief Account of a Century's Work. Published by H. K. Lewis and Company, Limited, London. Pp. viii plus 89. Illustrated. (Gratis.)

Report of the First S.M.S. Officers' Conference, Bombay Province, under the auspices of the Bombay Provincial Branch of the All-India Medical Licentiate's Association, Poona, 1946.

Abstracts from Reports

REPORT OF THE SCIENTIFIC ADVISORY BOARD, NEW DELHI, FOR THE YEAR 1945. ISSUED UNDER THE AUTHORITY OF THE GOVERNING BODY, INDIAN RESEARCH FUND ASSOCIATION, NEW DELHI, INDIA

THE report gives summaries of researches carried out in various centres under the authority of the Indian Research Fund Association. The work done during the year has shown that sulphaguanidine is of value in the treatment of cholera. It was given in 3-gramme doses every four hours for 3 days, and then twice a day for 3 days. In a series of 456 clinical cases of cholera the death rate was 2.1 per cent against 8.77 per cent in the control series. The enquiry is to be continued under field conditions as far as possible. At the Malaria Institute, Delhi, research activities were severely curtailed by abnormal conditions on account of the war. Six courses in malariology were held and attended by 147 military officers and assistants. A series of tests on monkey malaria have been carried out with paludrine (M 4888) which has shown considerable promise. Two indigenous drugs were tested, but were found to have no plasmodicidal value. A new blood stain has been developed, it can be used as a substitute for Romanowsky's stains and is more easily prepared from ingredients obtainable in India. A great deal of work has been done on D.D.T. emulsion and the development of equipment for its application. D.D.T. has been shown to be extremely effective against *A. minimus*, the chief malaria carrier of the foothills of Bengal, Assam and Burma, the residual effect persisting more than 2 months. Watery emulsions have been found to be more effective than oily solutions for spray killing of adult mosquitoes. An investigation is being made in the Punjab to evaluate the degree of association between rainfall and malaria. The interesting finding so far is that in a quite large number of districts rainfall in the month of May correlated significantly with the malaria epidemic figure of the following autumn, though the degree of relationship varies considerably from district to district. The cumulative effect of spleen indices of two or more previous years on the intensity of subsequent malaria epidemics is also under investigation. A great deal of preliminary work has been done to determine whether or not exo-erythrocytic cycle of parasite development occurs in Mammalian malaria. At Ratanpur in the Central Provinces where endemic filariasis is prevalent, an attempt is being made to control mansonioides, the transmitter of the infection, by removing *Pistia*, since in the absence of these plants the mosquitoes are

incapable of breeding. A number of drugs have been tested for their therapeutic value on filariasis, including penicillin. Of them, anthiomaline (lithium antimony thiomalate) proved helpful in the control of lymphangitis. Mapharside cleared up the urine in one case of chyluria, and filarsen (a combination of arsenic salt with killed TAB and streptococcal organisms) was thought to improve the general tone of the patients, but no drug had any effect

on the parasites in the tissues.

The work on nutrition was of varied nature and included some field investigations. An investigation on lathyrism in Bhopal State pointed to the fact that wheat procurement operations played a part in the genesis of the outbreak which was due to the consumption of lathyrus as a staple food for 6 months or more. Experimental results have not, so far, proved soya bean as superior to other pulses. The biological value of the proteins of food yeast has been determined. On an average it contains 51.75 per cent protein and rats gained much more in weight on rice diet and yeast than on rice diet without any supplement. Study of plasma proteins shows that there are types of cases in which the values of albumin and globulin can be accurately calculated from the value of total proteins by the application of certain formulae, thus saving much time and labour. Study of the effects of starvation was continued and completed during the year, the general picture at autopsy being congestion and degeneration in all the tissues, but more marked in the small intestine. In the more practical field the work done in Bombay is worth noting. The distribution of milk in the city and its suburbs is subsidized, and large numbers of people receive this article of food at 50 per cent concession rate. To meet the shortage, separated milk powder is being imported, and a farm has been started with 1,000 milk buffaloes. An experiment has been started in the mass feeding of unmarried personnel and recruits at the police headquarters at Thana, each man being charged Rs. 15 per month and the balance being met by the Government. Another community feeding experiment is being carried for the clerical staff at the Secretariat, a sum of nearly one lac of rupees having been spent on building, furniture and equipment. Yet a third experiment has been instituted in a rural area where students can join at a cost of Rs. 10 per month in community feeding which has already caused a distinct improvement in the health of those participating. School feeding continues to receive attraction of the Corporation of Bombay which spends nearly five lacs of rupees in giving free milk to undernourished children.

Field work confirms the observation that the greatest factor in the spread of leprosy is not casual contact but contact as a result of marriage. It appears that in South India leprosy is frequently a benign non-progressive disease in childhood, and that only a relatively small number of children who acquire the disease progress to the more serious forms. The policy of segregation practised in a village group since 1939 has reduced the incidence of the disease in three out of four villages. In the experience of one clinic the most efficient method of treatment is a combination of intradermal and subcutaneous injections.

A new field of the activities of the Board is in clinical research, a few subjects being included in this report. Work is progressing on deficient vitamin B complex utilization in oral cancer patients. A study of naga sore in Assam showed its incidence much higher in plantation labourers engaged in outdoor work than those engaged in indoor work in the factories. There was no evidence that an insect vector carried the disease, nor did dietetic factors seem to play any important part in the aetiology. One attack did not seem to prevent a subsequent one. A constant finding from the sore was fusiform bacillus, but a suspension of its culture, inoculated intracutaneously into a human volunteer, did not result in an ulcer. Results so far obtained indicate that the copper sulphate method of

estimating total proteins and the Biuret method of estimating protein fractions should be of wide applicability and utility in India. Preliminary studies of different methods of treating hypoproteinaemia have been made in about 20 patients. An investigation was conducted at Darjeeling into cases of bowel complaints. In several cases a new paracolon organism was isolated, but in many cases of atypical diarrhoea no pathogenic organism was found; there are however reasons for the view that some of them might be due to physical conditions affecting the gastro-intestinal secretions.

The Rh \pm states of 318 pregnant women attending the antenatal clinic of the Eden Hospital and 'suspected' families were examined. Their sera were also tested for intragroup reactions to detect any anti-Rh or anti-Hr bodies. (Anomalous intergroup reactions were also studied.) Three cases gave intragroup reactions, not due to anti-Rh bodies. 7.6 per cent of Indian women and 12.9 per cent of others (Europeans and Anglo-Indians) were found Rh negative. Anti-Rh animal sera of high titre were prepared in rabbits and guinea-pigs. Tube and slide methods in hæmo-agglutination for Rh were compared in a large number of cases. Comparisons were made with results obtained by the use of human testing sera.

Among the miscellaneous subjects, it is of interest to know that in Bombay and its suburbs all the three types of typhus infections corresponding to the three types of proteus X are met with. Response to treatment with proteolysed liver extract in uncomplicated tropical macrocytic anaemia was found to be of the same order as with patent injectable crude liver extract. The anthelmintic effects of combined butea and embelia, two indigenous drugs in ascariasis, compared very favourably with that of santonin or oil of chenopodium which is much more costly. An enquiry is proceeding into methods for the manufacture of penicillin and other problems connected with it.

R. N. C.

REPORT OF THE SUDAN MEDICAL SERVICE FOR THE YEAR 1944

THE state of public health throughout the year was satisfactory. Cerebro-spinal meningitis occurred as sporadic cases, only reaching epidemic proportions in certain parts of Equatoria. Smallpox was limited to only a small number of cases, though prevalent in the neighbouring countries, obviously due to the high degree of protection of the population by vaccination. The country was constantly exposed to the spread of typhus from Egypt for most of the year, but owing to strict quarantine and delousing of the exposed population, its incidence was almost negligible. There was no case of yellow fever; the campaign against *aedes* mosquitoes is now an important part of the work of the public health service. The only epidemic which caused worry was relapsing fever, whose incidence has considerably increased during the last few years and which necessitated the employment of a large staff for delousing and giving mobile treatment. There is some evidence that rectal schistosomiasis is increasing in the Gazira and may have possible effect on public health, for unlike urinary schistosomiasis it can become a serious disease. Legislation has been passed making notification and treatment compulsory. Kala-azar in the Sudan has still a large mortality, and attempts are being made to discover more effective lines of treatment. Malaria remained one of the major public health problems although there was on the whole a slightly lower incidence of the disease than in 1943. Anti-malaria work was extended further throughout the country. The incidence of venereal diseases also remained high, and it is considered that tuberculosis should be tackled as soon as possible.

The report gives an interesting summary of the improvement in public health in the Sudan during the last 48 years, an account of the work done in Stack Medical Research and Wellcome Chemical Laboratories, etc. The country is now in possession of a museum with 3,500 exhibits which should be of value

for teaching and propaganda. The sanitary services have been improved and several new maternity and child-welfare clinics were opened in the towns during the year. The number of hospital beds is well over 1 per 1,000 of the population. The medical budget is nearly 10 per cent of the budget of the Sudan.

R. N. C.

ANNUAL REPORT OF THE RANCHI EUROPEAN MENTAL HOSPITAL FOR THE YEAR 1944-45

UNDER an arrangement with the Government of India, 56 beds have been allotted for service patients, the medical and nursing personnel being provided from military sources. The total population of the hospital for the year was 461 (294 males and 167 females), the daily average being 258. Schizophrenia, neurosis and psychoneurosis, paranoid states and mental deficiency were the common causes of admissions. Electric convulsant therapy is used in some forms of mental disorder. Experience in this hospital shows that in schizophrenia if this treatment is given in early stage and continued until a full remission has been achieved, the beneficial effects are likely to be permanent. In affective states, particularly in the melancholies and depressive states, complete recovery has occurred in many cases after short courses of treatment. The results in psychoneurosis are encouraging. Of the probable causes of insanity mental stress occupied a prominent place. The majority of patients were between 20 and 40 years of age. Nearly 17 per cent were cured, 25 per cent improved, and 7 per cent died from various causes. The parole system has, as formerly, been extensively used, without any untoward occurrence.

R. N. C.

ANNUAL REPORT OF THE PURULIA LEPER HOME AND HOSPITAL OF THE MISSION TO LEPERS FOR THE YEAR 1945-46

THE number of inpatients was 682 and of outpatients 1,194. Of the total, 89 became symptom-free and 32 showed much improvement. One hundred and seventy patients have been permanently admitted into the colony. The Home had a difficult year from shortage of staff and supplies. The work of occupational therapy was extended by building a second weaving-shed for the women. Attempts are being made to grow more food by extending the areas of paddy fields and vegetable gardens. The home is dependent for 60 per cent of its income on voluntary gifts, and without this support its work would be greatly reduced in scope.

R. N. C.

Correspondence

VACCINATION FOR SMALLPOX

SIR,—A child aged three months was vaccinated against smallpox thrice at intervals of about two weeks. The lymph used on each occasion was quite fresh and obtained from very reliable sources. The vaccination each time was unsuccessful. No pustules appeared and no marks whatsoever have been left. Does this mean that the child possesses permanent immunity against smallpox not requiring further vaccination at any future date? Or is this immunity only of a temporary nature derived from the mother when in utero? If so, does the child require re-vaccination? After what intervals should this be done? If it is unsuccessful again should re-vaccination be permanently given up as unnecessary?

I shall be grateful to you for your opinion on the matter.

(Sd.) Illegible,

LIEUTENANT-COLONEL, I.M.S.,

Medical Officer,

King Edward Memorial Hospital,
Secunderabad-Deccan.

[The child is very probably not resistant (immune) but not susceptible to vaccine, that is to say the tissues have not yet matured to react. This phenomenon has been more extensively studied in diphtheria. It is possible that the child is also non-susceptible to variola but not necessarily so because intra-uterine smallpox is not unknown. However, there is, generally speaking, considerable age variation for maturation in reference to tissue susceptibility. If these premises are correct, the child will "take" when vaccinated later, say after six months. In the meanwhile greatest care should be taken to avoid exposure to specific infection.]

It will be interesting to follow this case and it may be instructive to see whether he reacts to other antigens. Perhaps response of the parents to antigens would be interesting as immunizability is believed to be an inherited characteristic.—R. B. L.]

Any Questions

SIR,—Is there any record in the available medical literature of any mumps case where suppuration of one or more of the salivary glands has occurred? I have recently seen a case where the right parotid gland suppurated subsequently although no clear evidence could be elicited to hold the mumps virus responsible for the suppuration.

Yours, etc.,
D. N. DEBSARMA,
Assistant Medical Officer,
Koilamari Tea Estate
Hospital.

NORTH LAKHIMPUR,
ASSAM.

[Suppuration of parotid glands in mumps *qua* mumps does not occur—a French author did not come across a single suppurating case amongst his series of 20,000 mumps cases. However as a complication due to secondary infection, it has been described by many authorities—see the following books:—

Price—'Textbook of the practice of medicine' (1946), page 176.

Greiffith and Mitchell—'The diseases of infants and children' (1938), page 347.

Garud, Batten, Thursfield and Patterson—'Diseases of children' (1929), page 939.

Rundle—'Ker's infectious diseases' (1929), page 515.

Stimson—'Common contagious disease' (1936), page 217.—R. B. L.]

SIR,—Is mepacrine hydrochloride excreted in the maternal milk, and if so, is it in a sufficient concentration to prevent malaria in the infant?

MEDICAL DEPARTMENT,
DOOM DOOMA AND ASSOCIATED TEA
COMPANIES, DOOM DOOMA
(UPPER ASSAM).

[So far as we are aware there is no record of observation on excretion of mepacrine in the milk. It is slowly absorbed, stored in the tissues and slowly excreted mostly by urine and faeces. It is not likely to prevent malaria in the infant through maternal milk.—R. N. C.]

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL N. M. P. DOTIVALA, M.C., Deputy Assistant Director-General (M. S.), Medical Store Depot, Lahore Cantt., is transferred as Deputy Assistant Director-General (M. S.), Medical Store Depot, Bombay, with effect from the forenoon of 20th April, 1946.

Major B. S. Khurana is appointed to act temporarily as Health Officer, Simla, with effect from the afternoon of the 3rd November, 1945, *vice* Colonel E. S. Phipson, C.I.E., D.S.O., I.M.S. (Retd.).

Major J. Goodall, on general duty at the Presidency General Hospital, Calcutta, is placed on general duty at the Medical College Hospitals, with effect from the 10th May, 1946, until further orders.

Major H. A. Ledger, an Agency Surgeon, on return from leave resumed charge of the duties of Civil Surgeon, Quetta/Sibi, with effect from the afternoon of the 31st December, 1945.

Captain D. H. Harrison, an Agency Surgeon, is appointed as Civil Surgeon, Zoh/Loralai, with effect from the afternoon of the 3rd January, 1946.

Captain R. Passmore, an Officer of the Medical Research Department, was transferred to foreign service under the Indian Research Fund Association, with effect from the 4th March, 1946, for temporary appointment as Director, Nutrition Research Laboratories, Coonoor.

LEAVE

On reversion to civil employ Major F. H. A. L. Davidson is allowed study leave for 6 months, on the recommendation of the Director-General, Indian Medical Service, under rule 1 of the Study Leave Rules for the Indian Medical Service.

Captain E. J. Somerset, Professor of Ophthalmic Surgery, Medical College, Calcutta, is granted leave on average pay for 4 months, with effect from the 1st May, 1946, or any subsequent date of availing.

PROMOTIONS

INDIAN MEDICAL SERVICE

Lieutenant-Colonel to be Colonel

A. N. Sharma. Dated 24th April, 1946.

Majors to be Lieutenant-Colonels

F. M. Collins. Dated 1st March, 1946.

D. P. Lambert. Dated 15th April, 1946.

26th February, 1946

P. H. Cummins.

W. J. L. Neal.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain to be Major

Bhabinadas Bhattacharyya. Dated 15th March, 1946.

Lieutenants to be Captains

8th November, 1945

M. Ahmad.

R. K. Khan.

M. S. Khan.

11th November, 1945

S. M. H. Bokhari.

K. Singh.

B. Prasad. Dated 12th November, 1945.

14th November, 1945

N. K. Mehra.

G. Singh.

K. Prasad. Dated 26th November, 1945.

A. S. Ramamoorthy. Dated 1st December, 1945.

A. M. Khan. Dated 27th December, 1945.

B. W. J. Ince. Dated 4th January, 1946.

5th January, 1946

M. Natarajan.

G. Venkataswami.

6th January, 1946

M. A. Jameel.

D. A. Lakshmanan.

S. P. Subramanian.

K. Purushothaman.

V. Anadaraman.

L. Sathyavageswam.

U. Sankaranarayanan.

G. Kuppuswamy.

B. K. Das. Dated 14th January, 1946.

P. Dharmaraju. Dated 20th January, 1946.

23rd January, 1946

K. V. Rao.

K. V. Subrahmanyam.

V. V. S. P. Rao. Dated 24th January, 1946.

25th January, 1946

P. Srinivasachari.

R. V. Row.

T. B. Tilak.

K. S. Rao.

J. Prasad. Dated 28th January, 1946.

INDIAN MEDICAL SERVICE

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY

(Emergency Commissions)

Lieutenants to be Captains

K. A. Malik. Dated 10th November, 1945.

M. Singh. Dated 21st November, 1945.

D. A. W. Nugent. Dated 4th January, 1946.
R. Tyagarajan. Dated 6th January, 1946.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY
MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

Lieutenant to be Captain

Mrs. B. J. Thorpe. Dated 15th January, 1946.

RELINQUISHMENTS

The undermentioned officers are permitted to relinquish their commissions on release from army service :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Ty. Lieutenant-Colonel P. A. Mathew. Dated 14th November, 1945.

Ty. Lieutenant-Colonel L. Oswald, 20th March, 1946, and is granted the honorary rank of Lieutenant-Colonel.

Ty. Major Z. A. Choudhuri, 21st March, 1946, and is granted the honorary rank of Major.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Major Rajeswar Bhattacharya. Dated 14th March, 1946.

Major B. S. Wagley. Dated 30th March, 1946.

Major V. K. Row. Dated 16th April, 1946.

Ty. Major H. L. Anand. Dated 14th February, 1946.

Ty. Major Asita Lal Som. Dated 24th March, 1946.

Major T. K. Chary. Dated 31st March, 1946.

Ty. Major H. S. Sinha. Dated 18th March, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major and his services are placed at the disposal of the Government of Madras, with effect from the date shown against his name :—

(Ty.) Major E. K. P. Nambiar. Dated 8th March, 1946.

The undermentioned officer of the I.M.S. (E.C.) reverts from the R.I.N.V.R., is permitted to relinquish his commission on grounds of ill health and is granted the honorary rank of Captain :—

Captain R. S. Velaskar. Dated 19th December, 1945.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain B. L. Nayar. Dated 15th March, 1946.

Captain V. R. Bagwe. Dated 19th March, 1946.

Captain A. R. Tampi. Dated 30th March, 1946.

Captain V. F. Siqueira, M.C. Dated 1st April, 1946.

Captain N. G. Chitnis. Dated 2nd April, 1946.

(Emergency Commission)

Captain K. B. Roy. Dated 2nd April, 1946.

Captain B. N. Roy. Dated 3rd April, 1946.

Captain A. B. Roy. Dated 8th April, 1946.

Captain D. I. Gantzer. Dated 13th March, 1946, and is granted the honorary rank of Captain.

The undermentioned officers are permitted to relinquish their commission on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain M. Imaduddin. Dated 23rd March, 1946.

Captain M. G. Nayar. Dated 14th April, 1946.

Captain A. J. Ralstol. Dated 24th March, 1946.

Captain T. Lazaro. Dated 1st October, 1945.

Captain J. J. Dharamraj. Dated 24th March, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain A. S. Choudhuri. Dated 26th March, 1946.

Captain A. Dhirar. Dated 19th April, 1946.

Captain S. Gopalaswami. Dated 9th April, 1946.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY
MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

Captain (Mrs.) N. D. Khanna. Dated 31st March, 1946, and is granted the honorary rank of Captain.

RESIGNATIONS

The undermentioned officers are permitted to resign their commissions :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Major S. Pichumani. Dated 13th March, 1946.

Captain I. Singh. Dated 19th March, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain M. P. Varma. Dated 8th February, 1946.

Captain S. Krishnamurti. Dated 30th March, 1946.

Captain J. R. Sen Gupta. Dated 4th April, 1946.

Captain Y. S. Bawa. Dated 15th April, 1946.

Captain M. P. Misra. Dated 19th April, 1946.

Captain S. K. Puri. Dated 26th April, 1946.

Captain S. B. P. Tawari. Dated 26th April, 1946.

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Original Articles

ARTERIO-VENOUS ANEURYSMS

CASE REPORTS

By H. R. PASRICHA

LIEUTENANT-COLONEL, I.M.S.

In the official history of the last war Sir G. Makins describes that in 1,004 injuries to the great arterial trunks he found some form of aneurysm in 545, or 54.4 per cent. In this war, no such comprehensive series has yet been published. With regard to comparative frequency, it was found that in a series of 272 cases there were 120 examples of arterial aneurysm, 100 of arterio-venous aneurysm and 52 aneurysmal varices.

Most surgeons, engaged in treating war wounds, must have come across such cases. The following cases are reported because of a special feature in each. In the first case the situation of the arterio-venous aneurysm was unusual and rendered radical treatment very difficult. In the second the special feature is the combination of extirpation of the lumbar sympathetic trunk with radical treatment of the aneurysm in an effort to avoid circulatory disaster to the limb.

Case 1.—R/M J. B. T., 2/5 G. Rifles, sustained grenade wounds of his right arm and right side of the neck behind the angle of the jaw on 27th May, 1943. An x-ray of right arm showed no fracture, but multiple metallic F.B.'s in the arm and fore-arm.

The notes received with the patient state that a peculiar thrill was noticed in the region of the angle of right jaw on 19th September, 1943.

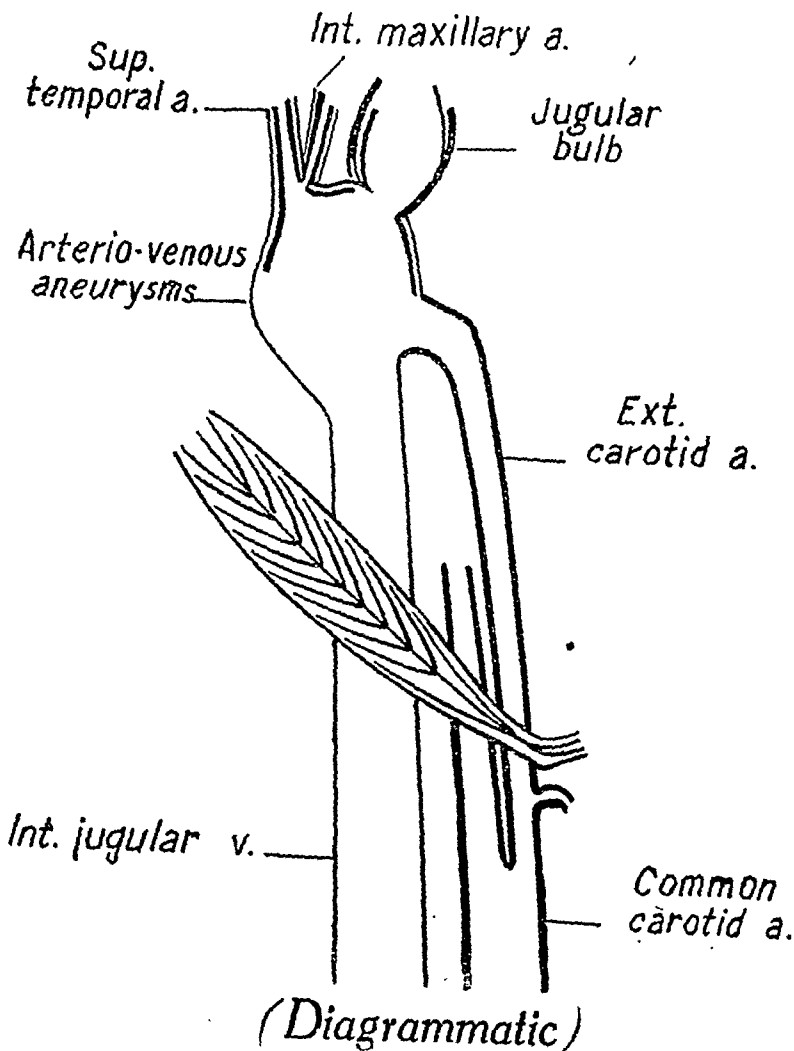
Case received on 18th January, 1944. Examination showed a complete right radial nerve palsy, a small healed scar in the right parotid region, well-marked congestion, and swelling of right half of the face particularly the parotid region. A thrill was palpable in the right half of face, temple and upper part of right side of the neck, most marked behind the angle of right jaw. A continuous rumbling murmur with accentuation in systole could be heard in the same areas with maximum intensity behind the angle of right jaw. Dilated veins showing a

tendency to tortuosity could be seen in the neck and temporal region. No cardio-vascular changes were detected nor any changes in the fundi. No involvement of any of the cranial nerves.

Patient was operated upon on 14th February, 1944, under gas and oxygen (intratracheal).

A curved incision was made below the angle of right jaw. External carotid artery was found and traced up towards the angle of jaw. Next the internal jugular vein was cleared. Both found to be joining a saccular enlargement above the posterior belly of digastric muscle. The sac was about the size of a large walnut situated about $1\frac{1}{2}$ inches above the point where hypoglossal nerve crosses the external carotid artery. The sac extended upwards deep to the parotid gland and was dissected free with difficulty. Internal maxillary and superficial temporal arteries could be seen leaving the superior convex border of the sac. Both the vessels were tied. Internal jugular vein and external carotid artery tied below the sac. The latter was too close to the jugular bulb to be excised. It was plicated and stitched.

Patient passed through a stormy post-operative period. The pulse rate kept high



(160/min.) for about six days before it finally settled down with the help of digitalin.

Patient kept under observation till 29th August, 1944, and then discharged completely cured. There was no sign of recurrence of the aneurysm. The swelling of the face had subsided. The situation and relations of the aneurysmal sac are shown in the diagram.

Case 2.—R/M S. R. L., 1/10 G. R., sustained a bomb splinter wound of his left buttock on 7th March, 1944. A small splinter entered into his left buttock and came out anteriorly just below the left inguinal ligament. Case received on 10th April, 1944.

On examination, a swelling about the size of a pigeon's egg in the femoral triangle just below the inguinal ligament was found. The swelling had a marked thrill and a continuous humming murmur with systolic accentuation. The thrill and the murmur disappeared on pressure over the femoral artery above the swelling.

There was no engorgement or dilatation of veins. No swelling or oedema of leg or foot. In addition he had a complete lesion of the peroneal division of the sciatic nerve. W.R.—negative. No lesion of the femoral or its branches.

No cardio-vascular changes.

Although there was no outward sign of circulatory disturbance in the limb, the risk of gangrene of leg following operation could not be disregarded. It was obvious that the femoral vessels may have to be ligatured high up.

To avoid this risk and facilitate the establishment of collateral circulation, it was decided to extirpate his lumbar sympathetic trunk before exploring the vessels.

Second to fourth lumbar ganglia with the intervening trunk were removed through an oblique incision in the loin (extraperitoneal approach) on 24th April, 1944.

Following the operation the skin temperature of the left leg rose several degrees and the limb became pinker than the right. On 28th May, 1944, the femoral vessels were explored through a vertical incision under spinal anaesthesia. The aneurysmal sac with all its radicals was exposed. The sac connected the femoral artery and vein about 1 cm. below the origin of the profunda femoris. This fortunate fact, difficult to predict before the operation, improved the prognosis considerably. A ligature of the femoral artery could not be so risky with the femoral profunda artery above it. Also, the profunda artery was much bigger in size than the superficial femoral artery. It appeared to be the more direct continuation of the femoral artery. Great saphenous vein also entered the sac. The sac was excised after ligaturing all the radicals. The wound healed by first intention and at no time was there any anxiety about the state of circulation in the limb.

The patient was discharged completely cured on 17th August, 1944, by which time his peroneal

nerve had made a complete spontaneous recovery.

Discussion.—Reid and McGuire (*Ann. Surg.*, 1938) recommended delay in operating upon arterio-venous aneurysms because a small one may close spontaneously.

In Carson's book, Grey-Turner recommends removal only for certain indications like pain, buzzing noises, increase in local distension of the vein, eye disturbances, cerebral symptoms, increase in size with aching and evidence of cardiac dilatation or embarrassment.

Delay in operation improves prognosis by allowing time for collateral circulation to develop. However, prolonged delay is known to lead to cardiac derangement more particularly if big vessels near the heart are involved.

Operation was not delayed in the first case because of this consideration and swelling of face which was increasing.

In the second case, it was apparent that high ligation of the femoral artery might become necessary which carries a distinct risk of gangrene of distal part of the limb. Even when gangrene does not ensue, the function of the limb is affected on account of circulatory disturbances like coldness, oedema on exercise or trophic changes. Lumbar ganglionectomy was performed to help the establishment of collateral circulation by removing the vaso-constrictor control of vessels.

* PSYCHIATRIC PRACTICE AMONGST INDIAN TROOPS

By KIRPAL SINGH

MAJOR, I.M.S./I.A.M.C.

Introduction.—These observations are based on my two years' experience as a psychiatrist in the army. During this period I have had the opportunity to treat and dispose of over 1,800 Indian personnel in a forward area in this theatre, i.e. 15th Indian Corps, in base hospitals in Ceylon and in the Advance Base Psychiatric Centre, Comilla.

Before coming to the actual psychiatric problems met with in these troops, I should like to mention a few points regarding the psychological make-up and social, cultural and religious background of the I.O.R. (Indian Other Rank) in general.

General background.—A vast majority of these men, mostly illiterate, come from villages and are farmers by profession. They are inclined to be fatalistic and believe that the time of one's death is fixed by Providence and is unalterable. This belief would appear to be an asset for soldiering especially in times of war. Religiously the main faiths professed are Hinduism, Islam and Sikhism, a small minority being Christians. A considerable number

* A paper read at the conference of 12th Army Psychiatrists at Rangoon on 11th November, 1945.

believes in the existence of ghosts and witchcraft and the efficacy of a charm, *tawiz* or talisman, in warding off the evil resulting from them. As a rule the I.O.R. is a stay-at-home type greatly attached to his family which in his case means not only his wife and children but includes, besides, his parents, brothers, sisters, cousins, uncles, aunts and many other relations as well. An Indian of this class considers presence at ceremonies such as marriage or betrothal of a relative a matter of the utmost importance, unlike the Westerner who may not consider it of great significance. In some cases, especially in the Punjab villages, more than one male member and in certain others all the eligible ones joined up, leaving practically nobody to look after the women folk, the children and the property.

The recruitment in the Indian Army is on a voluntary basis in the sense that there is no conscription in India, though pressure is in certain cases brought to bear through village headmen, many of whom acted as agents of the recruiting authorities in the area. Some joined up merely on account of economic necessity, others because of their family or racial tradition and some to prove their loyalty to the 'salt' they had eaten. But higher emotions like patriotism and fight for freedom could not be mobilized. They were unable to understand the Allied war aims or the implications of the Atlantic Charter, though consequent upon a prolonged training an 'esprit de corps' had developed in some who took pride in their comrades, their officers, their units and the regimental reputation. But such training, in case of many a recruit, failed to induce that state of mind in which the individual accepts that the success of one's unit, one's country and so on is more important in the scheme of things than oneself.

The I.O.R. considers leave as his right and cannot understand why he is not given leave when the domestic problems make his presence in his village imperative.

A large majority of the personnel, especially in the combatant units, comes from northern India, though during the present emergency a high proportion of men from the south was recruited for duties in AA regiments, sappers and miners, and other units which have proved their mettle in action.

Officers' position and training.—At the beginning of the war, with the huge and sudden expansion of the army, there was an acute shortage of officers having an experience of the Indian troops. Several young men had therefore to be commissioned after a comparatively short training. Also due to the very urgent military necessity several recruits who had hardly finished their training were thrown into action. The position, however, improved considerably towards the end of 1943.

Recruitment and selection.—The quality of the recruit seeking employment gradually

deteriorated and on account of the absence of a proper selection, the undesirables could not be eliminated in the first instance, therefore the time and equipment that was expended on such men had been wasted, in addition to the bad influence of these individuals on others. Constitutionally very poor specimens found their way into the units and a considerable time of the medical units was spent in boarding them out.

A sort of automatic selection, however, existed in the Indian Army, i.e. the Officers Commanding had the power to discharge an unsuitable soldier within the first six months of his service, without any formalities. This power was freely used to the great advantage of the army. Erroneous recruitment, e.g. enlistment as sweepers of men belonging to non-sweeper castes, caused a good deal of discontentment. It was quite common in the I.A.M.C. and raised several administrative difficulties.

Types of psychiatric cases met with.—Psychosis appears to be far more common than in the British troops probably due to the bad selection. Of the psychoneurotic breakdowns, anxiety states are rather uncommon and typical anxiety symptoms in the forward areas were seen only among the more sophisticated type of I.O.R., e.g. havildar clerks, V.C.O.s or the more intelligent N.C.O.s, while gross manifestations of conversion hysteria were comparatively more frequent.

Precipitating causes.—In addition to battle stress, physical disease played a very important rôle in the ætiology. Other conspicuous precipitating factors were domestic or unit difficulties, some grievance about promotion, non-availability of leave for a long time, and the loss of a *tawiz*. Illness of a parent or wife or some other distressing news from home, viz dispute regarding property, failure of family allotment to reach the allottee regularly, inability to go home when the date of one's own marriage or of a near relative had been fixed on an auspicious day after consultation with a priest, were prominent among the domestic causes.

One interesting fact about the psychotic reactions in the I.T. is worth mentioning, i.e. the condition is liable to change from day to day and what looks like a typical schizophrenic reaction may be recovered from in a few days' time. A considerable number of such cases received in the 15th Corps Centre were of toxic origin. Among the toxic ætiological factors malaria, undetermined febrile illnesses, amœbic dysentery, drugs like *Cannabis indica* and possibly mepacrine may be mentioned.

Two cases of toxic confusional psychosis will be described briefly to illustrate this point.

1. A Pathan from a Baluch Regiment was referred for refusal to take food, being depressed, muttering continuously and apparently hallucinated. At first sight it appeared

to be a schizophrenic reaction. On examination it was found that he had a temperature of 99°F., the spleen was just palpable and there were signs of meningeal irritation. The cerebro-spinal fluid, except for an increased pressure, showed nothing special. In spite of negative smears an intravenous injection of quinine was given and repeated after six hours. By the next morning the patient was almost normal and after completion of anti-malaria treatment he was discharged to his unit in ten days' time.

2. A Punjabi Musalman was treated for malaria B.T. in a M.F.T.U. and on the fourth day of treatment, i.e. second day of mepacrine when his temperature was normal, became confused, restless and hallucinated. He was transferred to the Corps Psychiatric Centre. The mepacrine was stopped and the patient put on quinine and sedatives. After two days his mental condition was normal. At this stage he was again switched on to mepacrine and the following day the confusional symptoms reappeared. The same phenomenon was observed in three more cases.

It has been mentioned in the literature that acridine dye products like atebrine, quinacrine and mepacrine have been known to produce confusional psychosis in some individuals. Dr. Seagrave makes a mention of it in his book 'Experiences of a Burma Surgeon' and the Americans in Ledo also described several such cases. Gaskill and Fitz-Hugh (1945) found that the total incidence of such psychosis, which complicate malaria cases treated with atebrine, was extremely small (0.4 per cent) and their course relatively benign.

A few cases of confusional symptoms due to Indian hemp and two following petrol drinking were seen. No symptoms of lead poisoning were seen in the latter though the army petrol is supposed to be leaded.

Several cases of pure physical illness with no or very little psychiatric accompaniments were received. Two examples will be given not with a view to criticizing the medical officers who sent them but only to show that gross physical disorders may be overlooked if a complete examination cannot be made, owing to rush of work or for any other reason.

1. A man, referred for somewhat odd behaviour, on examination was found to be suffering from one-sided complete 7th and 8th nerve paralysis, his behaviour having been due to his deafness and unshapely face.

2. A tall Sikh from a G.P.T. company, while cranking a motor engine, was struck by another truck on his back, and as he could not walk on account of pain he was admitted to a surgical ward. He was referred to me after a week as a case of hysteria. On examination I found some swelling and tenderness in the region of the left sacro-iliac joint, which prompted me to take

an x-ray and it was discovered that the man had a dislocation not only of the sacro-iliac joint but also of the symphysis pubis.

To mention some of the other somatic conditions, one or more cases of the following diseases were seen: scrub typhus, syphilitic meningo-myelitis, congenital heart disease with subacute bacterial endocarditis, pulmonary tuberculosis with cavitation, border line and frank malnutrition, and fracture of the lower end of ulna.

In another type of case the patient who has been off colour for some time reports sick at his M.I. room with vague symptoms like weakness and giddiness or as he would put it in Hindustani 'kamzori aur chakar ata hai'. He is given a dose of some mixture and sent back to duty. He tries to report sick once or twice again with no better luck. Ultimately when he is totally unable to carry on any longer, and as if to dramatize his illness some gross hysterical manifestation comes to his rescue and he is admitted to a medical unit where something grossly physical is discovered. To quote an example, a soldier from a Mahratta Light Infantry was received with the history of having had a fit while on parade, since when he developed paresis of both legs and complained of inability to walk. On examination he appeared very anæmic, hæmoglobin was 50 per cent, R.B.C. 2.5 million and blood picture showed microcytic hypochromic type of anæmia. Stools contained a large number of ancylostome ova. Rest, deworming and heavy doses of iron cured not only his anæmia but also the hysterical paralysis, and he was discharged to duty in about 6 weeks' time.

Having realized the importance of physical disease in the I.O.R. and found that even in those cases who suffered from a true psychiatric illness, some physical accompaniment was not uncommonly discovered, the following routine investigations were carried out in every case: record of temperature, B.S. for M.P., stools, E.S.R. and Kahn test.

Hysteria in most cases was motivated superficially by some domestic or unit difficulty. For instance a Gurkha youth was admitted for hysterical aphonia. Under pentothal narco-hypnosis it was discovered that he had been engaged to a girl for some years but could not marry her before joining the army, as he was not in a position then to pay the price asked for by her father; and when he had collected money he was not given leave. He was afraid lest his fiancée should be married to another man while he was away on active service.

Several cases of hysterical fits were attributed by the patients to the loss of a *tawiz* and were successfully treated by providing an 'improvised' one.

Analysis.—I have tried to analyse the first 100 cases seen in Arakan and the relevant figures are given.

A. *With reference to diagnosis.*—

Hysteria	..	17
Anxiety state	..	3
Mental deficiency	..	8
Psychosis	..	39
Toxic confusional state	..	12
Physical	..	21
		<u>100</u>

B. *Disposal.*—Twelve out of 20 psychoneurotics, i.e. 60 per cent, were returned to duty and of the 12 cases of toxic confusional states 10 were returned to duty either direct from the Corps Centre or after a period of convalescence in a Convalescent Depot or leave.

C. *Regional distribution.*—Of the 79 men suffering from psychiatric illnesses (excluding 21 cases of purely physical diseases) 32 came from South India giving a percentage of 40.5 per cent which appears to be considerably higher than the proportion of the South Indian in the army, but it should be mentioned that these men were from ancillary troops.

D. *With reference to the arms of service.*—

	Per cent		Per cent
Infantry	.. 26	Signals	.. 5
Artillery	.. 4	Medical	.. 10
R.I.A.S.C.	.. 19	Engineers	.. 18
Pioneers	.. 13	Ordnance	.. 5

The figures showing the relative strength of the various arms in the 15th Corps during that period (July to September 1944) are not available.

E. *Predisposition.*—As far as could be ascertained 13 out of the 79, i.e. 16.4 per cent, had a history of a family or personal predisposition.

F. *Relation to the military operation.*—It appeared that during the monsoon period when only patrol activity was going on the number that could be returned to duty was small. Similarly since the termination of hostilities a large percentage of patients have had to be evacuated.

G. *Miscellaneous data.*—

Average age	..	23
Average total service	..	2.5
Cases with some significant physical disease	..	38, i.e. 48.1 per cent
Marital status—		
Married	..	52 = 66 per cent
Single	..	26 = 34 per cent

Rank—		Per cent
V.C.O.s	..	3
N.C.O.s	..	10
Havildar clerks	..	10
Sepoys	..	53
Non-combatants	..	24

General.—The morale of the troops was high in the units officered by regular I.A. officers of some years' standing and having a well-organized welfare service and leave roster, while in non-combatant units it was rather low.

Summary.—The following points are brought out from the above observations:—

1. That the I.O.R. attaches very great importance to his village life and has a large number of dependants, whose welfare he has to look after.

2. That physical factors have an important place among the precipitating causes of psychiatric breakdowns.

3. That more careful selection at the time of recruitment, properly organized welfare service and leave roster, and sending the best medical officers as the unit M.O.s are among the important preventive measures.

Acknowledgments

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COBRA OR VIPER

By R. L. SPITTEL, F.R.C.S.

Is it possible, in a case of snake-bite terminating fatally, to say from the symptoms whether the offending reptile was a cobra or a Russell's viper?

The specific action of snake venoms (still imperfectly known) depends on ferments (proteolytic and fibrin), cytotoxins (acting on red cells, leucocytes, epithelium and nerve cells), agglutinins, cardiovascular toxins and neurotoxins. The neurotoxins predominate in the venom of colubrids, the cardiovascular toxins in that of the viperines.

Colubrine poisoning is characterized by rapidly advancing paralysis due to the action of the poison on the brain and cord—the muscles involved are usually those of the tongue, lips, throat, eyelids and limbs. Other symptoms are mental apathy, nausea and vomiting, and contracted pupils. Death is said to be due to paralysis of the respiratory centre. Coagulation nil, hæmorrhages nil—according to Rogers.

Viperine poisoning is characterized by hæmorrhages (local ecchymoses, hæmaturia, melæna) due to hæmolysis and intravascular clotting followed by incoagulability. Other symptoms are: collapse, thready pulse, nausea and vomiting, dilated pupils insensitive to light, and early loss of consciousness. Death is caused by paralysis of the vasomotor centre in the medulla. 'There is no paralysis of muscles...' (Manson).

But is the differential symptomatology between cobra and viper poisoning so clear-cut as to justify such assertions as that there are

no hæmorrhages in the former and no paralyses in the latter?

The case report shows that no such line can be drawn, for in it both paralyses (eyelids, tongue, pharynx) and hæmorrhages (gastric, rectal) co-existed.

F. Wall in 'The Snakes of Ceylon' says of cobra venom, after emphasizing the characteristic paralytic manifestations: 'Among other symptoms may be mentioned nausea or actual vomiting, and, not infrequently, hæmorrhages from various orifices as a result of the action of the poison on the blood, altering its composition, reducing its coagulability, and dissolving the red cells' (p. 487). In his illustrative case of the bitten punkah coolie, however, there is no mention of hæmorrhages from orifices. Regarding viperine poisoning, Wall is emphatic that, 'There are no paralyses as we see in colubrine toxæmia' (p. 518).

Wall's position then is that, while paralyses always characterize colubrine poisoning, there may also be hæmorrhages; in viperine poisoning, on the other hand, there are hæmorrhages but no paralyses.

The Military 'Manual of Tropical Medicine' is more guarded when it states: 'A given species of snake usually has venom that is predominantly of one type or the other, although more or less equal mixtures of the two occur in a few cases'. And this is perhaps the right view to hold.

Case.—S., a well-built Englishman of about 45, stepped out of his club at Colombo and was about to enter his car parked in a dark garage in the garden when he trod on a snake and received a bite. In the uncertain light, a large reptile 'yellowish-green' or 'khaki-coloured' was seen to glide hurriedly away. When the sock was turned down an electric torch revealed a single puncture just below the internal malleolus.

A few attempts having been made to squeeze out the poison, the patient was driven to a doctor who applied a tourniquet and incised the puncture under a local anæsthetic, but could induce very little bleeding.

I saw the patient at 10.30 p.m., about 1½ hours after he was bitten, and applied crystals of potassium permanganate into the open wound, followed by a compress of a saturated solution of magnesium sulphate to encourage bleeding. Except for slight pain about the ankle, the patient was in good spirits, and felt that unnecessary anxiety was being manifested over the bite of a harmless reptile, probably a 'rat snake', which seemed possible from the description of its great length. He insisted on going home instead of entering hospital.

At about 5 a.m. the following morning, his wife phoned up to say that he had spent a sleepless night and was complaining of great pain in the affected limb. He was admitted into the Nursing Home in a cold sweat, and complained of pain in the affected limb, epigastrium and

body generally. There was ptosis of both upper eyelids which he had to lift with his fingers to enable him to see. His pupils were normal and responded to light; there was no dimness of vision or diplopia. He was quite conscious and did not seem over-anxious about himself. His pulse, respiration, and blood pressure were normal. There had been some oozing of blood-stained serum into the compress covering the wound.

He next developed paresis of the tongue with difficulty of articulation (which partially improved in the course of the day) and of the pharynx, nearly choking himself in attempting to drink. Then followed a series of severe attacks of retching and hæmatemesis and the passing of blood per rectum, and later of mucus. There was no hæmaturia.

He was now becoming increasingly restless, and perspired profusely all the time. He kept jerking his injured leg violently, injuring it against the foot of the bed. Towards afternoon, his pulse became rapid and thready, his blood pressure dropped and his respirations became shallower, while his struggles were so violent that four persons could hardly control him. He did not quite lose consciousness until about 15 minutes before his death which occurred at 5 p.m., 19 hours after he was bitten.

Treatment.—He was given two bulbs of concentrated antivenene, one intravenously and the other subcutaneously—but this was not until the following morning, as the serum could not be obtained earlier. Saline and glucose intravenously, calcium, vitamin K, adrenalin and pituitrin were also administered. But none of these seemed to have the least effect.

Apart from the immediate application of a tourniquet and amputation where possible, such as of a finger or toe, there does not appear to be general agreement as to the best treatment of snake-bite. The Military 'Manual of Tropical Medicine' condemns the time-honoured use of alcohol and potassium permanganate. Even as regards incision, the Pharmacopœia of the Calcutta School of Tropical Medicine lays down, 'On no account should any incision be made'. While in the instructions supplied by the Central Research Institute, Kasauli (Punjab), we read, 'Make an incision at least ¼ inch deep over the fang wounds about one or two inches long and encourage bleeding to wash out the poison'—a counsel that should certainly not be disregarded as immediate treatment. (A lad I know was bitten between the thumb and index finger by a large Russell's viper that clung on and had to be forced off. He immediately applied a tight tourniquet, made two deep incisions over the fang marks, sucked out the wounds, and applied potassium permanganate. Even so, he soon became drowsy. His eyes were kept open with the use of pepper; he was walked about, and purged abundantly. For 24 hours he caused anxiety, but after that his recovery was rapid, dimness of vision persisting

for a few days. He consulted me three days later for the treatment of his wounds which gave little trouble.)

Identity of the reptile.—In the case I have described it was difficult to establish. The symptoms provided no clue whatever, paralyse and hæmorrhages co-existing. The snake, from the description of its size, was most probably one of two—a cobra or a Russell's viper—or possibly the much rarer Indian krait that grows to 4½ feet, the action of the venom of which is almost identical with cobra venom. Of these I myself think it must have been a Russell's viper for the following reasons:—

Russell's vipers were known to abound in the locality which was overgrown with scrub during military occupation; the description 'yellowish-green' is more applicable to the Russell's viper than the cobra, the cobra poises its hood and strikes downwards, while the Russell's viper, when trodden on, turns instantly and snaps like a dog; the single fang mark was a comparatively large one; the hæmorrhages (especially gastric) were a more prominent feature than the paralyse.

Considering that toxins affecting both the nerve cells and the blood elements are present in both colubrine and viperine venoms, there will probably always be cases where the predominant toxin, characteristic of one or the other, is levelled down.

TYPHUS IN RAJPUTANA.

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SINCE Megaw reported the first case of tropical (non-epidemic) typhus seen in India (1917), several hundreds of cases have been described from various parts of the country, the majority of which Roy (1946) collected and entered on a map of India. This survey as well as a perusal of available literature show that no cases of tropical typhus have been published from Rajputana. In this connection a remark by Hendley (1895) is of historical interest; in tabulating 'all other general diseases' which occurred in 'Jeypore' during his twenty years of service here, he states: 'Epidemics of typhus fever were reported as having occurred in the jail about 25 years ago. There have been none since'. This, obviously, was louse typhus and has nothing to do with the main problem of specifically Indian typhus which is still controversial as far as the vector or vectors are concerned.

To make sure whether unpublished cases of tropical (endemic) typhus have occurred in the neighbouring States of Rajputana, we inquired from the leading physicians of Alwar (Dr. Khatre), Bikaner (Dr. Weingarten), Jodhpur (Dr. D. N. Chatterjee) and Udaipur (Dr. Jaideo Prasad) whether they had seen any. The informations, kindly and readily supplied, were

negative; they had neither seen nor heard of typhus cases in their respective areas with the exception of Dr. R. J. Weingarten, Chief Medical Officer, Bikaner, who had diagnosed one such case. With his permission the following data are reported:—

S. S., a young cloth dealer, 18 years of age, was admitted to Bikaner Hospital in May 1945 with high fever and drowsiness. He showed a typical rash and petechiæ. On the 4th or 5th day of illness Weil-Felix reaction (Haffkine Institute, Bombay) showed the following result:—

OX19 negative
OX2 1:50 +
OXK 1:50 ±

Patient recovered in usual course of time without complications.

They thus proved that rarity of typhus cases in our part of India might justify the report even of a single case such as the following one:—

A. N., a well-to-do Brahmin, 40 years of age, who had not left Jaipur for many months, fell ill on 3rd March, 1946, with malaise, headache and fever of 101°F. which rose on the 2nd day to 103°F. and remained intermittent between 101°F. and 103°F. up to the 15th day of illness; between the 16th and 18th day the temperature gradually decreased and from the 19th day (22nd March, 1946) remained normal. During the first week he complained of restlessness, moderate pain in the limbs and diarrhoea.

I saw the patient for the first time on the 11th day of illness (14th March, 1946); his eyes were 'bloodshot' due to considerable hyperæmia of the conjunctivæ, pulse 120, temperature 102°F.; a maculo-papular rash covered the whole arms, the thighs and the upper half of the calves, the back and the buttocks, to a slighter extent the chest; face, hands and feet were free. A good many of the purplish-red macules and papules did not disappear on pressure due to capillary hæmorrhages which had developed since the rash was first noticed, three days prior to my being called for consultation, i.e. on the 7th or 8th day of illness. At that time the patient had taken a few tablets of cibazol so that the family doctor thought it was a drug rash.

During the following two days the rash spread to hands and feet, being clearly visible on the back of them and on the palms, but not on the soles; the face remained free. By the end of the third week the rash began to disappear but a good many of the hæmorrhagic eruptions changed to stained spots so that photographs taken on the 29th day (1st April, 1946) still showed them (see figures 1 and 2, plate XXIII).

Towards the end of the third week, along with the fading of the rash, a fine branlike peeling of the skin set in, especially on the extremities.

Heart, lungs and nervous system showed nothing abnormal; the liver and spleen were not enlarged. The urine contained an increased amount of urobilinogen; the stool was normal on microscopic examination. Before the rash appeared the blood was several times examined and found always negative for malarial parasites. Leucocyte count: 15,000 with 78 per cent neutrophils, 20 per cent lymphocytes and 2 per cent large monocytes (10th day).

On the 11th day of illness blood serum separated under aseptic conditions, sealed in sterile ampoules, was sent to Haffkine Institute, Bombay, for carrying out the Weil-Felix test. Dr. S. R. Savor found the following agglutination titres:—

Proteus OX19: 1/50 +; 1/125 +; 1/250 +; 1/500 ±; 1/1,250 negative.

Proteus OX2: 1/50 +; 1/125 negative.

Proteus OXK: 1/50 negative.

Two weeks later, on the 25th day from the onset of illness (28th March, 1946), seven days after the temperature had become normal, the Weil-Felix test was negative (Dr. D. W. Soman, Haffkine Institute).

Treatment was symptomatic, and directed to increase the patient's general resistance by giving high amounts of vitamins, para-aminobenzoic acid being not available here. Recovery was quick, uneventful and complete.

Of the usual vectors, louse and mite can be excluded in this case. The former because of the spotless cleanliness of the patient and his family, the clinical course, the distribution of the rash and the coagglutination of OX2 which hardly is found in louse typhus. The absence of agglutinins for OXK excludes the mite as vector. A high titre for OX19 and a low one for OX2 could be found in flea and in tick typhus.

To decide whether rat fleas or ticks should be incriminated proved here as difficult as in our former investigations (Heilig and Naidu, 1941, 1942). The patient stated that rats were present in his home; our attempts to trap them failed. On the other hand, he was building a dairy farm, kept cattle in his house and frequently went to the grazing places near the city to inspect his cows and buffaloes. I picked some two dozen ticks from 2 cows, kept in his courtyard, and sent them to Haffkine Institute where on 1st April, 1946, two guinea-pigs and 4 mice were inoculated with a ground suspension of 4 ticks; one of the guinea-pigs died on the 19th day after inoculation without showing any pathological signs on post-mortem examination, whereas the other inoculated animals were still alive and apparently healthy on 23rd April, 1946 (Dr. Soman). The other ticks Dr. Savor took to Kuala Lumpur (F.M.S.) for further investigation.

Summarizing, we have to say that this case of typhus which occurred in Rajputana resembled clinically in every point the cases reported from Mysore (Heilig and Naidu, *loc. cit.*).

Bloodshot eyes, character and duration of fever, the well-developed rash which leaves pigmented spots and its distribution all over the body with the exception of the face, good prognosis and speedy recovery—all these points were characteristic also for most of the 32 cases observed in Mysore. Complement fixation tests, performed in three of the Mysore cases, were highly positive for Rocky Mountain spotted fever (Topping, Heilig and Naidu, 1943; Heilig and Naidu, 1944), results almost proving that the Mysore vector is a tick. In the present case, on the other hand, the titre for OX19 was ten times higher than that of OX2; this, taken together with the negative results of animal inoculations with our ticks, may point to the rat flea as the responsible vector rather than to tick-typhus where the agglutinins for the various proteus strains are more equally distributed. But from a single case with only one positive Weil-Felix test definite conclusions cannot be drawn.

My thanks are due to Lieut.-Colonel Sir S. S. Sokhey, I.M.S., Drs. S. R. Savor and D. W. Soman, Haffkine Institute, and to Dr. Prabhu-Dayal, Jaipur, who called me in for consultation.

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A SIMPLE METHYLENE BLUE-EOSIN SUBSTITUTE FOR LEISHMAN AND GIEMSA STAINS

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THE modifications of Romanowsky stain, commonly used in this country, are Leishman and Giemsa. During World War II, these stains became scarce, and were not readily available to workers in India. Intensive work to develop a suitable substitute which could be prepared in the laboratory from materials available in India was undertaken and results of these investigations are presented in this paper.

The Romanowsky stain consists of two parts: the dye and the solvent. The dyes usually employed are methylene blue (or its derivatives) and eosin. When watery solutions of these

dyes are mixed together, dissociation of their respective ions occurs resulting in the formation of new compound or compounds (methylene blue-eosinate), a phenomenon analogous to salt formation. Since this is insoluble in water, it is precipitated. If this precipitate is collected and dissolved in methyl alcohol and is used as a blood stain, it fails to produce the desired Romanowsky effect. If, on the other hand, eosin solution is added to a methylene blue solution previously prepared (a few weeks or months earlier), the precipitate is found to possess adequate staining properties, showing its special affinity for staining the chromatin of the malaria parasite a characteristic red colour, as a result of oxidation of methylene blue. This process can be hastened if a freshly prepared solution of methylene blue is heated in the presence of an alkali. The staining properties are considered to lie not in the methylene blue solution itself but in a new compound called methylene-azure, which is formed as a result of the oxidation of methylene blue.

In the preparation of the new substitute the principles adopted by Wilson (1907), Stévenel (1918), and Krueger and Proescher (1924) who successfully polychromed a solution of methylene blue by using strong oxidizing agents as accelerators have been followed. It was found that not only can polychroming be quickly achieved, but that the formation of azure-eosinate and other compounds responsible for staining are not in any way hampered by the presence of suitable oxidizing agents. In fact a suitable compound giving all the effects of metachromatic staining can be easily and rapidly obtained. Many experiments, using different concentrations of these dyes and oxidizing agents in different proportions of water, were carried out, and the formula finally adopted as the most satisfactory one is given below :—

Methylene blue (medicinal B.P.)	..	1.0 gm.
Potassium permanganate (medicinal)	..	0.3 gm.
Water-soluble yellow eosin (B.D.H., London)	..	0.4 gm.
Water, distilled or tap	..	250 c.c.

Preparation of the Stain

Divide 250 c.c. water into 3 parts : 100 c.c., 100 c.c. and 50 c.c. Dissolve 1.0 gm. methylene blue in one lot (100 c.c.) of water in a flask, and in another 0.3 gm. potassium permanganate. The water need not necessarily be distilled, for slightly alkaline tap water with a pH value of 7.2 to 7.6 has been found to give satisfactory results.

When the methylene blue is completely dissolved, transfer the solution to a porcelain dish, heating it over the direct flame of a bunsen burner, or a spirit lamp. Allow it to steam but not to boil for about five minutes. Add gradually to this steaming blue solution, the potassium permanganate solution. A fine

layer of crystals forms on the surface. Continue heating the mixture for some 10 minutes or so. In the remaining 50 c.c. water, dissolve 0.4 gm. eosin and add it to the steaming methylene blue-permanganate mixture. Mix the contents thoroughly by stirring with a glass rod. A thick yellow scum appears on the surface. Continue heating for an hour or longer till the solution in the dish has evaporated, leaving behind a thick scum with a metallic lustre, at first copper red in colour and when dry green. Care should be taken not to heat the mixture too strongly. The residue in the porcelain dish should be left overnight in a desiccator or in an incubator at 37°C. When completely dry, the scum will peel off as shining green flakes. If necessary, these may be removed by means of a scalpel. Powder the flakes in a dry glass mortar and store the powder thereafter in a dry airtight glass container.

Use of this Powder as a Substitute for Leishman Stain

Take 0.1 gm. of the stain powder, place it in a glass mortar and dissolve it thoroughly by grinding it in 40 c.c. methyl alcohol added in small quantities at a time. The grinding process should be continued till all undissolved particles go into solution. Transfer the contents to a small bottle without filtering. Solutions of the stain made from different batches of powder prepared in these laboratories have retained staining properties for many months, giving excellent results.

The technique of staining blood smears, both thick and thin, is identical with that followed in Leishman's method.

Use of the Powder as a Substitute for Giemsa Stain

The same powder can be used as a substitute for Giemsa stain. Take 0.3 gm. of powder, place it in a glass mortar and grind it adding very gradually a mixture of glycerine and methyl alcohol (25 c.c. each). The freshly prepared solution should be placed in a small glass bottle and allowed to remain at room temperature overnight. On the following day, place the bottle neck deep in a water bath for about 2 hours.

The staining technique in this case is identical with that followed in Giemsa's method and the results achieved have been as good as with any of the standard stains.

Summary

A simple and inexpensive method of preparing a substitute for Leishman and Giemsa stains from dyes readily available in India has been described.

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THE [^]ROLE OF SYNTHETIC FOLIC ACID (*L. CASEI* FACTOR) IN THE TREAT- MENT OF NUTRITIONAL MACROCYTIC ANÆMIA

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IN 1941, Mitchell, Snell and Williams extracted a substance from spinach, acidic in nature, having a molecular weight of 500 and containing nitrogen but no sulphur and phosphorus. This substance or one with similar chemical and physiological properties is present in a number of animal tissues, the best sources being liver and kidney. It is also present in mushrooms and yeast and is rather abundant in green leaves including grass. Because of this last fact and also as the substance appeared to be a nearly pure chemical entity the authors suggested the name folic acid for it (from Latin *Folium* meaning a leaf).

Folic acid was reported to stimulate the growth of *Lactobacillus casei* (*helveticus*) in the same way as the various other factors previously reported, viz *Norite eluate* factor (Snell and Peterson, 1940; Hutchings and Bohonos, 1941), *Vitamin Bc* (Pfiefner *et al.*, 1943), *L. casei* factor from liver (Stockstad, 1943), *L. casei* factor from a fermentation residue (Hutchings, *et al.*, 1944). But folic acid differs from some of these factors in the degree of biological activity and also chemically as it does not contain any phosphorus.

In 1945, sixteen investigators, Angier *et al.*, announced the synthesis of folic acid, and almost immediately Spies, Vilter, Koch and Caldwell (1945) reported the results of the first clinical trial of synthetic folic acid in the treatment of macrocytic anæmia. They found that in 9 cases of macrocytic anæmia, administration of folic acid by mouth or parenterally was followed by a striking hæmopoietic response, as is seen after potent liver extracts. Later, Vilter, Spies and Koch (1945), on further studies in 15 cases of macrocytic anæmia, reported that with intravenous administration of the drug in daily doses of 20 mg. for 10 to 26 days as also with oral administration in 100 mg. doses daily for 10 to 30 days, evidence of regeneration of blood was noted in all the cases but the final hæmoglobin and red cell values were always sub-maximal. From the results obtained in the cases treated so far, they observed that in the doses given folic acid does not produce reticulocytosis and red cell increase as great as that induced by adequate dose of potent liver extracts given parenterally. They

concluded that synthetic folic acid could not be expected 'to have a curative effect above and beyond that offered by potent liver extracts since the original compound was isolated from the liver'.

Successful treatment of macrocytic anæmia in non-tropical sprue, in pernicious anæmia and in other conditions with folic acid, is also reported by Darby and Jones (1945), Spies *et al.* (1945), Moore *et al.* (1945), Darby, Jones and Johnson (1946), Doan, Wilson and Wright (1946), Spies *et al.* (1946) and Goldsmith (1946). The results obtained by some of the workers, e.g. Moore *et al.* and Doan *et al.*, were very satisfactory and were attended with good reticulocyte response. According to Doan and his colleagues, 'the results obtained in the case of Addisonian pernicious anæmia with synthetic *L. casei* factor, Lederle, seem thus far to parallel in all respects the response to liver therapy'.

Recently Spies *et al.* (1946) again tried folic acid on 45 cases of very rigidly selected macrocytic anæmia and reported that the administration of synthetic folic acid, either by mouth or parenterally, is followed by a prompt hæmopoietic response in persons with Addisonian pernicious anæmia, nutritional macrocytic anæmia, macrocytic anæmia of pregnancy, pellagra and the macrocytic anæmia of sprue. Spies did not find folic acid to be effective in iron deficiency anæmia, aplastic anæmia or leukaemia. A tentative dose of 20 mg. by mouth or parenterally was suggested by Spies.

Selection of cases of the present series.—The cases were selected rigidly after careful physical and laboratory examinations according to the criteria laid down by Spies *et al.* (*loc. cit.*), viz (1) The anæmia was definitely macrocytic in type and the initial red cell count was less than 2.5 millions; as a rule most of the cases had a red cell count of less than 1.5 millions. (2) The patient did not have any complicating disease which might be lethal during the course of study. (3) The patient did not have any recent treatment for anæmia. (4) The bone marrow was cellular and megaloblastic in reaction.

Method of study.—All the patients were admitted into the Carmichael Hospital for Tropical Diseases and were kept in the hospital during the whole period of treatment. The patients, except nos. 6 and 7 who was a strict vegetarian, were given the ordinary hospital diet containing approximately 90 grammes of protein of which about 60 grammes were of animal origin. Case no. 7 though a strict vegetarian consumed about 1½ seers of milk a day, while case no. 6 was intentionally put on a low protein diet.

Cases with the initial red cell count of one million or less were put on the folic acid treatment within a day or two of admission into the hospital, but cases with red cell counts of 1.5 millions or over were not put on treatment without subsequent examination of blood to exclude

improvement which sometimes follows rest and diet in the hospital.

Sternal puncture and gastric analysis were done in all cases. Detailed clinical and laboratory examinations were also carried out to exclude any associated infection.

During the period of stay in the hospital detailed examination of blood was done once a week.

Reticulocyte counts were done almost daily from the 3rd day of folic acid treatment till it returned to about the normal level.

All the hæmatological examinations were carried out according to the technique advocated by Napier and Das Gupta (1946), and Israels' (1939) nomenclature was followed in describing the immature cells of the red cell series.

Estimation of serum protein was done by micro-Kjeldahl method in the Biochemical and Diabetes Research Department of the School.

Method of administration.—In all cases, powder synthetic folic acid, Lederle, was given by mouth in gelatin capsules. The total dose for the day was given in two equally divided doses.

CASE RECORDS

Case 1.—I., a male, aged 26, a sweeper, was admitted with complaints of weakness and breathlessness on exertion. The patient looked very pale. The face was puffy and the tongue pale and flabby. Slight œdema was present in the ankles and feet. The spleen was not palpable but the liver was just palpable. The heart was slightly dilated and hæmic bruits were heard over the mitral and pulmonary areas. No abnormality was detected in the lungs and in the nervous system. Blood pressure was 95/60.

Laboratory findings.—Blood picture—see graph 1.

Sternal marrow—hyperplastic and predominantly megaloblastic (see table I).

Fractional gastric analysis—absolute achlorhydria.

Blood chemistry—total protein 3.8 per cent; alb./glob. 2.9/1.9; cholesterol 0.125 per cent.

Wassermann reaction—positive.

Stool—no protozoa or ova found.

Urine—nothing abnormal.

Treatment.—Folic acid, 100 mg. daily, was given for 10 days, it was omitted for 7 days and again given in 20 mg. dose for 10 days. It was again omitted for 10 days and was given for the third time in 20 mg. dose for 14 days. In all 1,480 mg. of folic acid were given in course of 51 days. Acid mixture* was given twice daily.

* *Acid mixture:*

R Acid hydrochloric dil. 3p

Glycerine pepsin 5i

Aqua ad 5i

Sig. To be taken in a cup of water with the two principal meals.

The mixture was given to all cases of achlorhydria and hypochlorhydria during the period that the patients were in the hospital.

At the end of folic acid treatment the patient was given proteolyzed liver extract* 100 gm. daily for 10 days. During the latter part of his stay in the hospital the patient was given a few injections of bismostab. After discharge from the hospital he was taking a course of treatment for syphilis in a V.D. clinic.

Results.—Clinically the patient showed considerable improvement; hæmatologically also there was steady though slow improvement up to a certain point. Tolerably good reticulocytosis, 27.4 per cent, was noted on the 5th day. Even at the end of 46 days' treatment with folic acid, mean corpuscular volume was slightly above the normal range. With proteolyzed liver extract, the red cells had increased by more than half a million and the mean corpuscular volume came well within the normal range. The total leucocyte count had gone up from 4,800 to 8,700 after folic acid treatment.

The patient was again examined at the end of 40 days, after some anti-syphilitic treatment, when his blood picture was found to have returned to the normal level.

Case 2.—J. A., Hindu male, aged 30, Behari, office servant, came with the complaints of anorexia, flatulence and progressive weakness. The patient looked pale and the face was puffy. The spleen was enlarged about 2 inches and was soft in consistency. The liver was also enlarged about 2 inches. The heart was slightly dilated. No abnormality was detected in the lungs or in the nervous system. Blood pressure was 105/60.

Laboratory findings.—Blood picture—see graph 2.

Sternal marrow—cellular and definitely megaloblastic in reaction (see table I).

Fractional gastric analysis—hypochlorhydria.

Blood chemistry—total protein 4.9 per cent; alb./glob. 3.6/1.3; cholesterol 0.095 per cent.

Wassermann reaction—positive.

Stool—trophic and cystic forms of *E. histolytica* present.

Urine—nothing abnormal.

Treatment.—Folic acid was given in a daily dose of 20 mg. for 30 days. During the latter part of the stay in the hospital when his blood picture had improved considerably he was treated for amœbiasis and was also given a few injections of bismostab. Acid mixture was given twice daily.

Results.—The patient improved remarkably both clinically and hæmatologically. There was moderate reticulocytosis, 18 per cent on the 5th day and increase of leucocyte count from 3,200 to 5,600 per c.mm. at the end of folic acid treatment. After the treatment with folic acid was discontinued, the blood picture continued to improve, lost its macrocytic character, and

* Proteolyzed liver extract (P.L.E.) given to this case as also to case nos. 3 and 4 was prepared in this laboratory.

reached the normal level within 20 days. Subsequent examination of the blood about one month after discharge from the hospital showed still further improvement.

Case 3.—J., Hindu widow, aged 36, maid-servant, was admitted with complaints of extreme weakness, breathlessness and palpitation on exertion. She was treated for macrocytic anæmia in this hospital in 1941, attended the anæmia clinic from time to time for the treatment of macrocytic anæmia in 1942, 1943 and 1944, and was treated in the Calcutta Medical College Hospitals in 1945 with liver extract. She had been suffering from bleeding piles for the last 2 years.

The patient looked slightly pale. There were evidences of superficial glossitis. Slight koilonychia was found in a few nails of the hand. The spleen was just palpable and the liver could be felt $1\frac{1}{2}$ inches below the costal margin. The heart was slightly dilated but nothing abnormal was found in the lungs. Blood pressure was 95/60.

During the second course of treatment with folic acid the patient complained of a dragging pain in the right leg. On examination a slightly anæsthetic patch was found over the dorsal aspect of the middle of the right leg. Left knee jerk could not be elicited. Finger-nose test was found to be defective with eyes closed. Gait was ataxic and Romberg's sign was positive. The diagnosis of subacute combined degeneration of the cord was corroborated by Dr. C. Saha, Neurologist, Medical College, Calcutta, while Dr. Dharmendra, Leprosy Research Worker at the School, supported our contention that the anæsthetic patch was not due to leprosy.

Laboratory findings.—Blood picture—see graph 3.

Sternal marrow—very cellular and highly megaloblastic in reaction (see table I).

Fractional gastric analysis—absolute achlorhydria.

Reference to old notes showed that the patient had megaloblastic marrow and absolute achlorhydria in 1941.

Blood chemistry—total protein 4.5 per cent; alb./glob. 2.3/2.2; cholesterol 0.110 per cent.

Wassermann reaction—negative.

Stool—no protozoa or ova found.

Urine—nothing abnormal.

Treatment.—Folic acid was given in doses of 100 mg. daily for 7 days and then in 20 mg. doses for 11 days. After an interval of 10 days it was given in doses of 20 mg. for 8 days. The patient thus received 1,080 mg. of folic acid in course of 36 days. Two weeks after folic acid treatment she was given proteolyzed liver extract 100 gm. daily for 7 days and later liver extracts (Lilly and T. C. F.) parenterally. Acid mixture was given twice daily.

Results.—The patient showed considerable improvement clinically, but hæmatologically improvement was rather slow. There was

tolerably good reticulocytosis, 18.1 per cent, on the 6th day of the first course of folic acid treatment. The blood picture continued to be macrocytic even at the end of the second course of folic acid treatment. Examination of blood 14 days after cessation of folic acid treatment showed considerable fall in the red cell count and the blood picture again became highly macrocytic in character. Administration of liver was followed by increase in the red cell count and hæmoglobin value and lowering of the mean corpuscular volume. The leucocytic count had increased from 3,200 to 6,900 per c.cm. at the end of folic acid treatment.

Case 4.—Mrs. J. S., Hindu female, aged 18, nullipara, housewife, was brought from Assam with complaints of progressive anæmia, breathlessness and anasarca. The patient looked very pale, the face was puffy and the tongue pale and slightly coated. There was marked œdema in thighs, legs and feet. The spleen was not palpable but the liver was just palpable. The heart was slightly dilated and soft systolic murmur was heard over the mitral and pulmonary areas; the first sound was rather weak. Blood pressure was 90/60.

Laboratory findings.—Blood picture—see graph 4.

Sternal marrow—cellular and megaloblastic (see table I).

Fractional gastric analysis—absolute achlorhydria.

Blood chemistry—total protein 4 per cent; alb./glob. 1.8/2.2; cholesterol 0.075 per cent.

Wassermann reaction—positive; Kahn—negative.

Stool—no protozoa or ova found.

Urine—trace of albumen only.

Treatment.—Folic acid, 30 mg. daily, was given for 30 days. 300 c.cm. of stored citrated blood was transfused on the 4th day of folic acid treatment. At the end of folic acid treatment proteolyzed liver extract was given, 100 grammes daily for 14 days, and later Lilly's crude liver extract 4 c.cm. intramuscularly daily for 5 injections and subsequently on alternate days up to another 5 injections. Acid mixture was given twice daily.

Results.—The patient did not show any improvement clinically for the first 4 days of folic acid treatment, but took a turn for the better after the transfusion. Since then she showed steady improvement clinically and hæmatologically up to a certain point. There was 26.6 per cent reticulocytosis on the 6th day of the folic acid treatment. At the end of folic acid treatment the leucocyte count had gone up from 3,900 to 6,500 per c.mm.

Only slight improvement was noted after liver treatment.

Case 5.—S. M., Hindu male, aged 22, Behari durwan, came under observation with complaints of breathlessness on slight exertion, weakness,

and frequent loose stools with blood and mucus. The patient gave a history of an attack of dysentery 2 years ago. The patient looked very pale and showed signs of wasting. The tongue was pale and moist. The spleen was not palpable but the liver was just palpable. Nothing abnormal was found in the heart, lungs and in the nervous system. Blood pressure was 100/70.

Laboratory findings.—Blood picture—see graph 5.

Sternal marrow—very cellular and definitely megaloblastic (see table I).

Fractional gastric analysis—absolute achlorhydria.

Blood chemistry—total protein 3.8 per cent; alb./glob. 2.5/1.3.

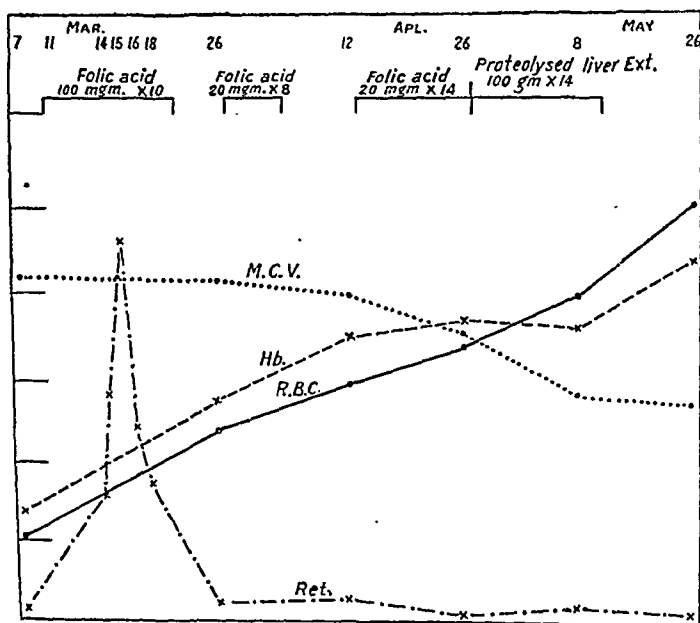
Wassermann reaction—negative; Kahn—doubtful.

Stool—no protozoa or ova found.

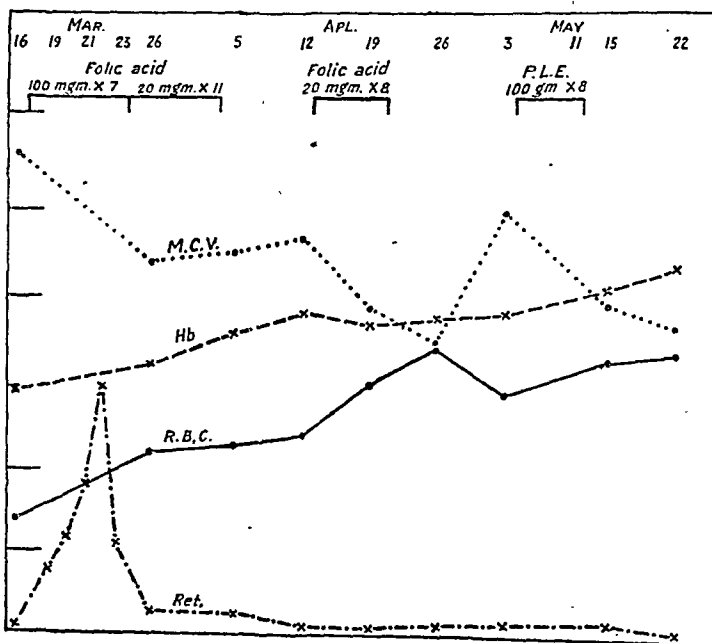
Urine—traces of albumen only.

Treatment.—Folic acid 30 mg. daily for 28 days. At the end of folic acid treatment 4 c.c. of liver extract (Lilly) was given intramuscularly daily for 5 days and later on on

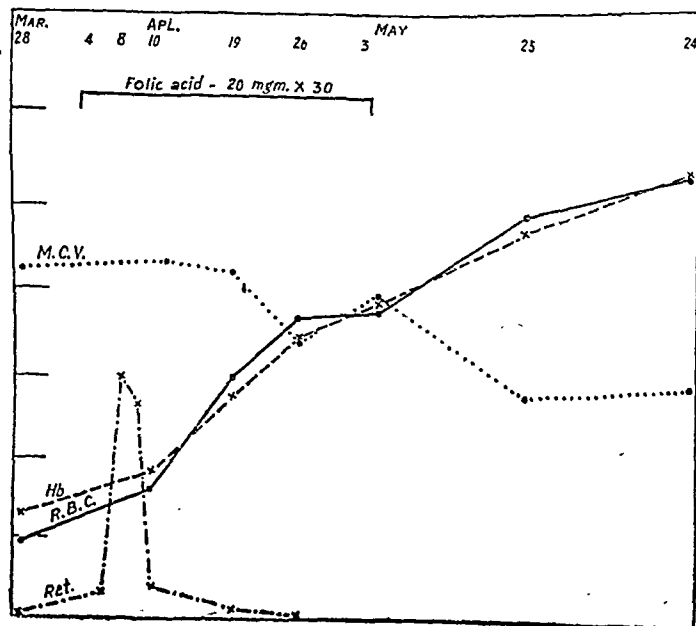
Graph 1.



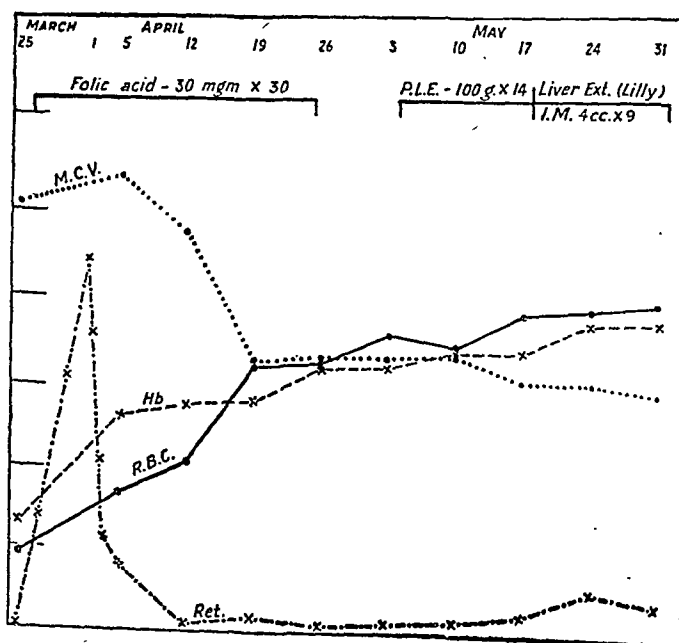
Graph 3.



Graph 2.



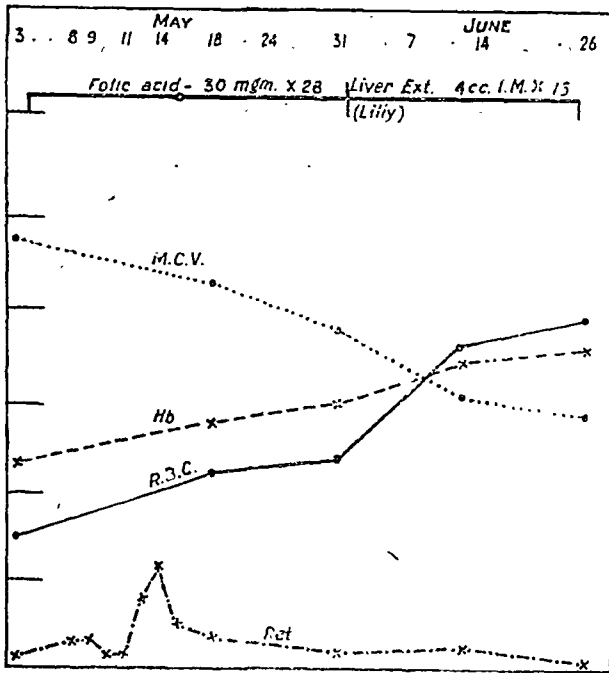
Graph 4.



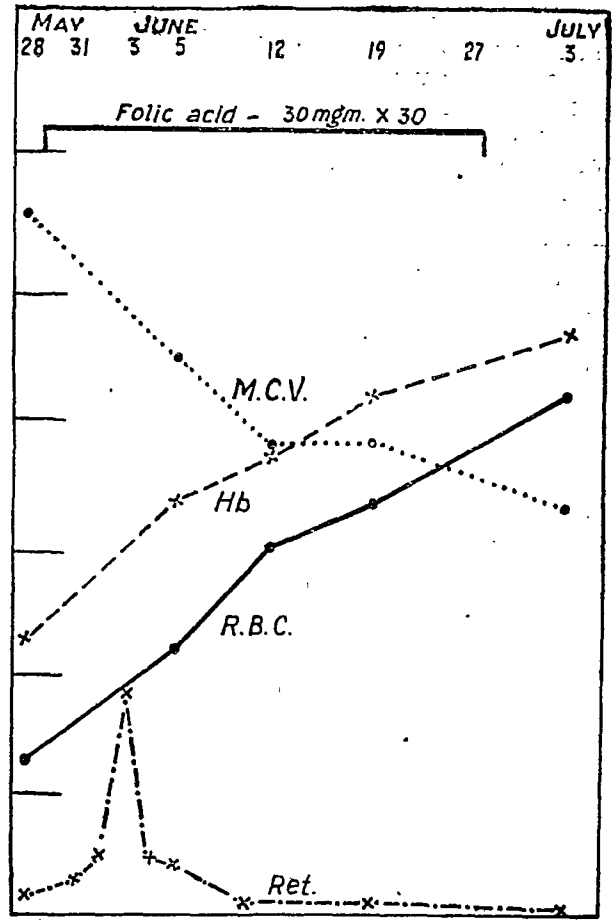
Each division on the ordinate denotes :—

R.B.C. 1 million; Hb. 3 gm.; M.C.V. 30 cu.μ; reticulocytes 6 per cent.

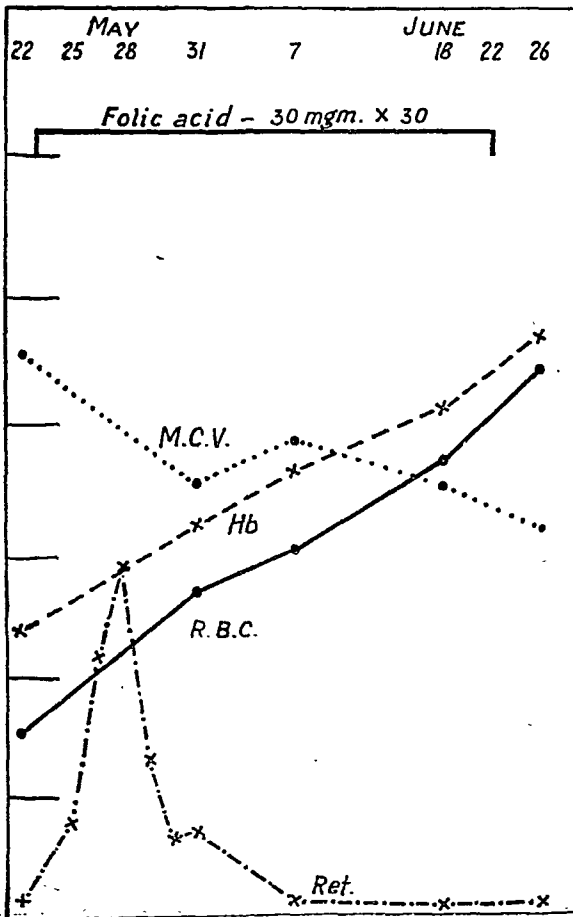
Graph 5.



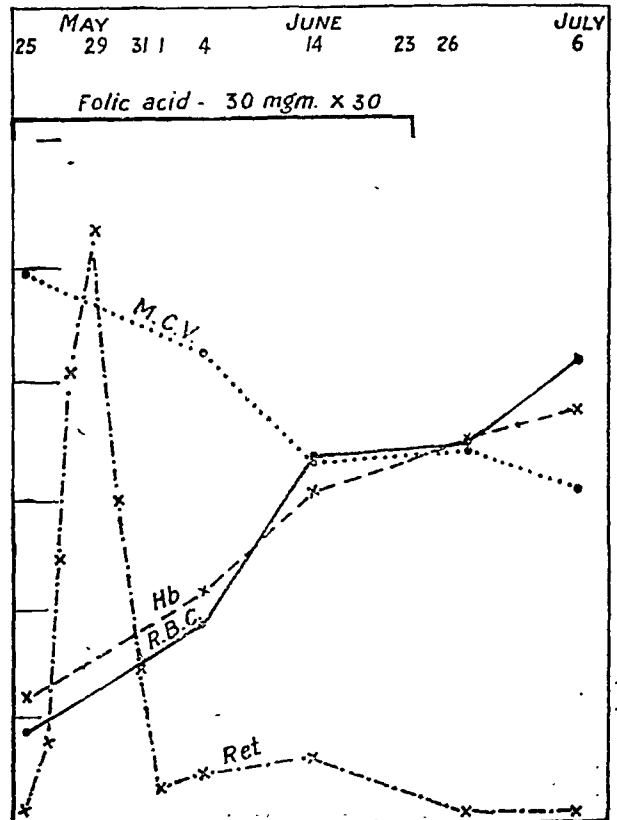
Graph 7.



Graph 6.



Graph 8.



Each division on the ordinate denotes:—

R.B.C. 1 million; Hb. 3 gm.; M.C.V. 30 cu.μ; reticulocytes 6 per cent.

alternate days up to another 10 injections. Acid mixture was given twice daily.

Results.—The patient showed considerable improvement clinically, but hæmatologically the response was not satisfactory; reticulocytosis was poor. Institution of liver therapy at the end of folic acid treatment showed further improvement in the blood picture. The blood picture continued to be macrocytic in type during the folic acid treatment but lost the macrocytic character after a few injections of liver.

Temporary increase in the white cell count was noted once during the course of folic acid treatment which again fell down to about the pre-treatment level.

Case 6.—G. S. S., Hindu male, aged 25, Behari, office servant by occupation, was admitted with complaints of slow fever, anorexia, weakness and giddiness. He gave a history of malaria 2 years ago. The patient was pale and looked very weak and ill. Spleen was enlarged one inch; liver was also enlarged one inch. Heart was slightly dilated with apical systolic bruit. Nothing abnormal was found in the lungs or in the nervous system. Blood pressure was 100/50.

Laboratory findings.—Blood picture—see graph 6.

Sternal marrow—highly cellular with megaloblastic reaction (see table I).

Fractional gastric analysis—pseudo-achlorhydria.

Blood chemistry—total protein 6.4 per cent; alb./glob. 4.0/2.4; cholesterol 0.120 per cent.

Wassermann reaction—negative.

Stool—no ova or protozoa was found.

Urine—nothing abnormal.

Treatment.—Folic acid 30 mg. daily for 30 days.

Results.—Patient showed steady and progressive improvement, both clinically and hæmatologically. There was moderate reticulocytosis, 17.6 per cent, on the 6th day. The blood picture reached the normal values and lost its macrocytic character after 30 days' treatment with folic acid. No change in the total and differential leucocyte count was noted during the course of treatment with folic acid.

Note.—To eliminate the hypothesis that hæmopoiesis might be caused by the protein contained in the average hospital diet, the patient was put on a low protein diet; fish, egg and meat were completely excluded from the diet and the only source of his animal protein was half a seer of milk. The patient was getting approximately 65 gm. of protein daily of which only 13 gm. was of animal origin.

Case 7.—B. S., Hindu male, aged 26, Marwari, a businessman by occupation and belonging to lower middle class, was admitted with complaints of giddiness and palpitation on slight exertion. The patient was a strict vegetarian from birth. He looked ill and the face was pale and puffy. There was slight œdema in the ankles. The tongue appeared slightly glazed at the tip. The spleen was not palpable but the liver just

palpable. The heart was slightly dilated with apical systolic bruit. Nothing abnormal was found in the lungs and in the nervous system. The blood pressure was 100/60.

Laboratory findings.—Blood picture—see graph 7.

Sternal marrow—cellular and megaloblastic (see table I).

Fractional gastric analysis—hypochlorhydria.

Blood chemistry—total protein 4.5 per cent; alb./glob. 1.3/3.2.

Wassermann reaction—positive; Kahn—positive.

Stool—hookworm ova 500 per c.c.

Urine—nothing abnormal.

Treatment.—Folic acid 30 mg. daily for 30 days. Acid mixture was given twice daily.

Results.—The patient showed excellent improvement clinically and hæmatologically. There was moderate reticulocytosis, 11.2 per cent, on the 6th day. Though the red cell count and hæmoglobin had reached almost the normal level at the end of folic acid treatment, the blood picture was still slightly macrocytic in type.

Case 8.—N. D., unmarried Hindu female, aged 20, belonging to lower middle class, was admitted with complaints of irregular fever, breathlessness and palpitation on slight exertion and œdema of legs.

The patient had an attack of epidemic dropsy 1½ years ago. She was dyspnoic and looked very ill with œdema all over the body. She had impetigo on left leg and on the scalp. Examination of the tongue showed evidences of slight superficial glossitis. The spleen was not palpable but the liver was enlarged about 2 inches and was tender. The heart was dilated with weak 1st sound. In the lungs fine crepitations were heard at both bases. Nothing abnormal was found in the nervous system. Blood pressure was 98/60.

Laboratory findings.—Blood picture—see graph 8.

Sternal marrow—very active marrow, slightly megaloblastic reaction (see table I).

Sternal puncture in this case was done on the third day of folic acid therapy.

Fractional gastric analysis—hypochlorhydria.

Blood chemistry—total protein 4.3 per cent; alb./glob. 2.8/1.5; cholesterol 0.100 per cent.

Stool—giardia cysts; ascaris ova 500 per c.c.

Urine—very faint trace of albumen.

Treatment.—Folic acid 30 mg. daily for 30 days.

Results.—The patient showed rapid improvement both clinically and hæmatologically. Reticulocyte response was good, 31.9 per cent on the 5th day. At the end of folic acid treatment, the blood picture was below the normal level and slightly macrocytic in type, but soon after cessation of the treatment, the blood picture lost its macrocytic character and was well within the normal range. With folic acid treatment the white cell count increased from 1,300 to 4,300 per c.mm.

TABLE I
Sternal puncture results

Number	Total nucleated cells per c.mm.	Granular cells. per cent	Non-granular cells. per cent	Red cells. per cent	Pro-erythroblast. per cent	Megaloblasts. per cent	Normoblasts. per cent
1	283,000	41.6	11.60	46.8	0.0	38.0	8.8
†2	Cellular	37.5	8.75	53.75	0.5	28.5	24.95
†3	"	26.0	3.40	70.6	0.0	44.4	26.20
†4	"	46.25	12.25	41.5	0.0	21.5	20.00
5	236,000	49.8	14.2	36.0	0.0	28.0	7.6
6	399,000	34.4	7.0	58.6	0.2	26.4	32.0
7	157,000	37.0	11.0	52.0	0.0	17.6	34.4
*8	295,000	10.8	2.0	87.2	0.2	2.4	84.6

† Total cell count could not be done but the examination of the smears showed that the marrow was more cellular than normal.

* Sternal puncture was done on the 3rd day of folic acid treatment.

Comment.—Of the 8 cases treated with folic acid, appreciable improvement, clinical and hæmatological, was noted in 7 cases and slight improvement in one (no. 5). Generally along with the increase in the red cell count and hæmoglobin value, increase in the white cell count was also noted. The improvement in all the cases was preceded by reticulocytosis, which was quite good in 3 cases (nos. 1, 4 and 8), moderate in 3 others (nos. 2, 3 and 6), tolerable in one (no. 7) and poor in one (no. 5). Except in case 8, where the reticulocyte response and the subsequent improvement was good, and in case 5, where both reticulocyte response and subsequent improvement was poor, there does not appear to be any correlation between the degree of reticulocytosis and rate of improvement in the other cases.

In most cases, clinical and hæmatological improvement was not attended with immediate lowering of the mean corpuscular volume which continued to be slightly high even up to the end of folic acid treatment. In 4 cases (nos. 1, 3, 4 and 5) liver was given after folic acid. Administration of liver was attended with further improvement in the hæmoglobin value and/or in the red cell count and in most cases the improvement was attended with lowering of the mean corpuscular volume.

Excepting case 5, which did not respond well to folic acid, the improvement seen in the 5 cases (nos. 2, 4, 6, 7 and 8), where folic acid was given continuously for 30 days in small doses of 20 to 30 mg. a day, was much better than the improvement seen in the 2 cases (nos. 1 and 3) where the drug was given interruptedly for about the same period or longer, in big doses of 100 mg. a day for the first one or two weeks and later in 20 mg. doses a day with short intervals between the courses, though the total amount of folic acid given to cases in the latter group was greater. The degree of reticulocytosis in one of the cases getting 100 mg. of folic acid a day (no. 1) was high, but not higher than what

was seen after 30 mg. dose in 2 cases (nos. 4 and 8).

In all the cases the bone marrow, as determined by the sternal puncture, was found to be more cellular than normal. It will be noted that the best response with folic acid was seen in the cases where the immature cells of the red cell series constituted more than 50 per cent of the total nucleated cells of the marrow, and the least response was seen in the case showing the lowest nucleated red cell count, case no. 3 being an exception. It will also be noted that generally better response was noted in the cases where the bone marrow, though megaloblastic in reaction, showed a fair amount of normoblastic erythropoiesis than in the cases where the bone marrow was predominantly megaloblastic in reaction.

Generally, the cases with absolute achlorhydria (nos. 1, 3, 4 and 5) did not show as good improvement as the cases which were capable of secreting acid even in small amount after alcohol meal alone (nos. 2, 7 and 8) or after histamine (no. 6).

The total protein was low in all cases except case 6. The lowering of the protein was due to decrease of both albumen and globulin fractions in 4 cases (nos. 1, 2, 5 and 8) and due to decrease of albumen only in the remaining 3 cases (nos. 3, 4 and 7). Generally, the cases with total serum protein over 4.0 grammes per cent showed better improvement than the cases whose serum protein was 4.0 grammes per cent or less, case 3 again being an exception.

The improvement with folic acid does not appear to be influenced by the pre-treatment dietetic habits of the patients so long as the patients had adequate calories during the course of treatment. Also the improvement does not seem to be influenced by the protein intake of the patient, specially protein of animal origin during treatment, as will be seen in case 6, provided the total protein intake was not below the physiological minimum.

Associated infection with syphilis in cases 1 and 4, with syphilis and *E. histolytica* in case 2, with syphilis and hookworm (500 ova per c.c. of stool) in case 7, with ascaris in case 8, does not appear to have seriously impeded the rate of improvement with folic acid treatment.

Discussion

All the cases in the series, except case 3, are typical cases of nutritional macrocytic anæmia. The frequent relapse of macrocytic anæmia in the absence of any maintenance treatment with liver, together with the associated neurological symptoms in case 3, strongly suggests that she may be really a case of Addisonian pernicious anæmia. But pending further investigations, we have included this case in our series as a case of nutritional macrocytic anæmia.

Though the number of cases treated with folic acid is small, the results are so striking, in the majority of the cases, that a brief comparison between the results obtained in cases of nutritional macrocytic anæmia with synthetic folic acid in the present series, and those obtained with liver extracts in the past (Napier *et al.*, 1939); Das Gupta, 1943; Das Gupta, Ganguly and Chatterjea, 1946) is given below :

Regeneration of blood after folic acid was always quick in all cases except one, case 5, and appeared to be quicker than what is generally seen after liver therapy, parenteral or oral. The increased activity in the marrow was reflected in the peripheral circulation at first by reticulocytosis and later by increase in the red cell count and hæmoglobin value. Reticulocytosis after folic acid was a constant feature and was generally of a higher magnitude than what is usually seen after potent parenteral liver therapy; reticulocytosis being rather poor after oral administration of proteolyzed liver extract. Maturation of the red cells, however, did not appear to proceed with equal rapidity, at least in all the cases, as the formation of new red cells, as a result of which the mean corpuscular volume, in many cases, did not come down within normal range, even after 30 days' treatment with folic acid. This is very seldom the case after successful treatment with liver, oral or parenteral.

It has already been mentioned that case 5 did not respond well to folic acid treatment but responded better to liver treatment. In this case as well as in the other cases, 1, 3 and 4 where liver was given after folic acid, some lowering of the mean corpuscular volume was noted after liver therapy.

It would thus appear that the deficiency factor or factors in nutritional macrocytic anæmia cannot always be fully made good by folic acid alone. It would also appear that there are probably two factors which are essential to bring about a remission in nutritional macrocytic anæmia, one of the factors being responsible for stimulating more accelerated

formation of new red cells while the other factor is responsible for proper maturation of the red cells.

It is more than probable that liver contains both the factors and probably in equal proportion. It is also probable that the two factors are also present at least in small amount, in marmite and in the diet, but it is possible that in both the maturation factor is the predominating factor. In view of the good results obtained with folic acid in cases of macrocytic anæmia and also in view of the fact that the original compound was isolated from liver, it is probable that synthetic folic acid, Lederle, also contains both the factors. But it is possible that in the folic acid, the stimulating factor is present in excess of the maturation factor. This would explain the persistence of macrocytic character of the blood picture in some of our cases, in spite of improvement in the red cell count and hæmoglobin value.

After folic acid treatment an increase in the white cell count was noted in most of our cases. In one case (no. 5) the increase in the white cell count was noted even in the absence of any appreciable improvement in anæmia. Increase in the white cell count, after folic acid treatment, was also noted by Vilter, Spies and Koch (1945), Darby, Jones and Johnson (1946), Doan, Wilson and Wright (1946), Spies *et al.* (1946) and by Goldsmith (1946). Whether the increase in the white cell count in the anæmic cases was due to increased vascularity of the marrow following improvement in anæmia or whether this was due to the direct action of folic acid on the leucopoietic tissue, is rather difficult to say at the present moment. It is probable that the stimulating action of folic acid is not confined to erythropoietic tissue alone but folic acid may, under certain conditions, stimulate leucopoiesis as well. This contention is supported by the works of Berry, Spies and Doan (1945).

Summary

1. Eight cases of nutritional macrocytic anæmia with megaloblastic reaction of the marrow were treated with synthetic folic acid given by mouth. Appreciable improvement was noted in 7 cases and slight improvement in one. In most of the cases, increase in the white cell count was also noted.

2. The improvement was generally preceded by reticulocytosis.

3. Oral administration of small daily doses of 20 to 30 mg. given continuously for 30 days seemed to have better effect than when given interruptedly in big doses of 100 mg. a day for the first week or two and though the total amount was more.

4. The mean corpuscular volume continued to be slightly macrocytic in type even up to the end of folic acid treatment.

5. Administration of liver in 4 cases subsequent to folic acid treatment was attended

with further improvement which was appreciable in one case but slight in the other 3 cases.

6. Generally, better response was noted in the cases where the bone marrow though megaloblastic in reaction showed a fair amount of normoblastic erythropoiesis than in the cases where the bone marrow was predominantly megaloblastic in reaction.

7. The cases with absolute achlorhydria did not show as good improvement as the cases with hypochlorhydria or pseudo-achlorhydria.

8. Generally, the cases having total protein more than 4.0 grammes per cent showed better improvement than the cases whose serum protein was less.

9. Pre-treatment dietetic habit or the amount of protein in the diet during the course of treatment with folic acid did not seem to influence the improvement of the cases.

10. Associated infection with syphilis, histolytica or mild infection with hookworm did not appear to seriously impede the rate of improvement with folic acid treatment.

11. The improvement with synthetic folic acid in properly selected cases of nutritional macrocytic anæmia did not appear to be inferior in any respect to what is generally seen after potent liver extracts, oral or parenteral.

Acknowledgment

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SEROLOGICAL TECHNIQUE (contd.)

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DETERMINATION OF THE TYPE OF BLOOD

M and N Hæmogens

THE type depends on these hæmogens which are quite unrelated to the isogens A and B, and occurs as M, N or MN in all subjects of all groups. No subject, unlike the subject O in the O-A-B system, is free from them. They differentiate three types in each group and thus make possible 12 descriptions of blood. A blood may be :

OM	ON	OMN
AM	AN	AMN
BM	BN	BMN
ABM	ABN	ABMN

If two subgroups A_2 and A_2B are included 6 more descriptions, 18 in all, become possible.

The hæmogens M and N have also been called, cryptically and unnecessarily, M and N 'Factors.'

Testing Fluids

They are the anti-M fluid and the anti-N fluid which are prepared in rabbits from known OM and ON bloods.

Collection of OM and ON bloods.—OM and ON bloods from professional donors are collected in Rous and Turner's solution, as recommended by Wiener (*loc. cit.*), as follows : 3.8 per cent sodium citrate solution, in lots of 20 c.c., is sterilized in 100 c.c. flasks; 5.4 per cent glucose, in lots of 50 c.c., is sterilized in 250 c.c. flasks; 30 c.c. of blood from a donor are drawn, added to the citrate solution, and the whole added to the glucose solution. The mixture is kept in a refrigerator. Fifteen c.c. of a packed deposit of rbc can be obtained from the 100 c.c. of the mixture. Required quantities can be withdrawn with a 10 c.c. pipette. Strict sterility must be maintained. The mixture remains fit for use for over two months. A slight or even marked

colour in the supernatant fluid can be ignored and so may be darkening of the deposit, as long as there is no smell, turbidity or other signs of bacterial growth.

The mixture is centrifuged and the supernatant citrate and glucose solution removed. The deposit is washed once in sterile saline. These operations are done in rubber-capped centrifuge tubes when the rbc are required for injection. For absorption the capping of the tube is not necessary.

Injection of rabbits for anti-OM and anti-ON sera and collection of the sera.—Full-grown rabbits weighing about 3 lb. (the usual weight of a rabbit purchased in Calcutta) are injected intravenously with a 50 per cent suspension of the rbc as follows:—

1st injection	..	1 c.c.
2nd injection, on the 4th day	..	1 c.c.
3rd injection, on the 8th day	..	2 c.c.
4th injection, on the 12th day	..	4 c.c.

(This is an old scheme which gave good results. The scheme detailed under Rh for the preparation of the anti-Rh serum may also be tried.)

Ten days after the last injection the animals are bled. The serum is distributed in lots of 1.25 c.c. in small phials which are corked and sealed with paraffin, inactivated, and stored frozen (in the freezing chamber of a refrigerator).

Absorption of anti-OM and anti-ON sera with O and obtaining of the residual anti-M and anti-N fluids. (i) *Absorption of anti-OM serum.*—So far we have found that a good serum when diluted 1 in 25 (two drops of serum, from the calibrated pipette, added to 1 c.c. of saline from which two similar drops have been removed, make a 2 in 50 dilution. Addition of an equal volume of saline gives a 1 in 50 dilution. Higher dilutions of 1 in 100 and 1 in 200 are obtained, if desired, by the same process of doubling volume) agglutinates both rbc OM and ON in an equal volume of a 2 per cent suspension in 30 minutes. The clumps of the OM rbc appear more compact in comparison with those of the ON cells. None of our sera has agglutinated the O rbc in a 1 in 50 dilution.

One c.c. of the serum (or a little over, as much as can be removed from the phial) is added to 1 c.c. of a packed deposit of ON cells in a 15 c.c. centrifuge tube and the two mixed by gentle tapping and rotation. The rbc are agglutinated into a gelatinous mass. The tube is left in an almost horizontal position in a moist chamber, for half an hour at room temperature, for half an hour in a refrigerator, and for half an hour again at room temperature. It is then centrifuged and a clear fluid (with or without a tinge of colour) measuring 0.1 c.c. to 0.2 c.c. more than the serum added (due to a tighter packing of the rbc) separated.

One drop of the absorbed fluid is tested with one drop of a 2 per cent OM rbc. If agglutination commences in about two minutes and is complete in five minutes the potency is regarded as good.

One, two and three drops of the absorbed fluid are next tested, on a slide marked into three compartments, with one drop of a 2 per cent ON rbc. If no agglutination occurs in any of the compartments in 30 minutes the specificity of the fluid is regarded as good.

If agglutination (definite or even a granularity) occurs with one; two or three drops, the specificity is defective. The serum must be reabsorbed with 1 c.c. to 0.5 c.c. (depending upon the degree of the agglutination); of packed ON rbc. The reabsorption does not lower the titre for OM rbc.

The absorbed fluid of a good potency and specificity is the anti-M fluid. It is collected with a capillary test pipette, transferred to a phial, and preserved with 0.25 per cent tricresol. For the purpose of adding tricresol volume of the antifluid is looked upon as 1 c.c. One drop of tricresol, from the calibrated pipette, added to 0.14 c.c. of ether = 1 in 8 of tricresol. A drop of the mixture added to 1 c.c. of anti-fluid gives the desired 1 in 400 (8×50) or 0.25 per cent. One c.c. of the fluid suffices for 40 to 50 tests.

(ii) *Absorption of anti-ON serum.*—The serum when diluted 1 in 100 to 1 in 200 agglutinates both rbc OM and ON in equal volume of a 2 per cent suspension. The ON rbc are made more compact in comparison with the OM cells.

The serum is diluted 1 in 4 to 1 in 8 with normal saline, the rest of the procedure is the same as described for the absorption of the anti-OM serum, with OM substituted for ON.

The reabsorption of the anti-ON serum with OM rbc lowers the titre for ON rbc also. The finished anti-N fluid, however, acts as briskly as the anti-M fluid, the reason being that a 1 in 4 dilution of a serum found agglutinating perfectly in a 1 in 100 dilution and giving a \pm reaction in the next higher dilution is stronger than the pure serum which agglutinates in a 1 in 25 dilution but not in a 1 in 50 dilution. The discrepancy is due to the inequality of spacing in the geometrical series, 1/25, 1/50, 1/100, 1/200.....

The Technique of Typing

The procedure is similar to the one followed in grouping a suspension of rbc with known sera, a and b.

In the left-hand compartment of the slide use a drop of anti-M fluid and in the right-hand compartment a drop of anti-N fluid. Add a drop of the unknown suspension, mix and leave in the petri dish.

If only anti-M fluid agglutinates, the type is M.
 " " anti-N " " the type is N.
 " both fluids agglutinate, " the type is MN.

Read the results in 5 minutes, 15 minutes and 30 minutes. After 15 minutes no new change occurs. A suspension giving a \pm reaction in 5 minutes and not progressing further is retested.

with 2 drops of the fluid. A + reaction is obtained in most cases.

DETERMINATION OF THE Rh +/- STATE OF BLOOD

The Hæmogen

It is found normally in the rbc of the Indian brown monkey, *Macacus rhesus*, the Rh are the first two letters of the specific name. It is also found in most humans. Only some humans (between 7 and 10 per cent in India, about 15 per cent in Europe and America) are without the hæmogen: they are Rh—, others being Rh+. The hæmogen Rh is independent of the isogens A and B and hæmogens M and N.

Each of the 12 or 16 bloods, described under M and N, may be Rh + or Rh—, e.g. OMRh+ (also written OMRh) and OMRh— (also written OMRh). The hæmogen is detected by specially prepared animal sera or sera of women who have given birth to babies suffering from erythroblastosis foetalis.

Preparation of an Animal Testing Serum

Rabbits are immunized as for the production of a hæmolytic amboceptor from the rbc of the brown monkey, according to the following plan:—

- 1st intravenous injection of 1 c.c. of 50 per cent rbc.
- 2nd intravenous injection of 1 c.c. of 50 per cent rbc on the 2nd day.
- 3rd intravenous injection of 1 c.c. of 50 per cent rbc on the 3rd day.
- 4th intravenous injection of 1 c.c. of 50 per cent rbc on the 4th day.
- 5th intravenous injection of 1 c.c. of 50 per cent rbc on the 5th day.

On the 5th day after the last injection a small sample of blood is collected in a capillary pipette from the ear vein. The serum from the sample is inactivated in a capillary pipette at a 56°C. for 1 hour ($\frac{1}{2}$ hour does not suffice for the complete destruction of the complement). From it are prepared two dilutions: a 1 in 500 dilution and a 1 in 1,000 dilution.

One drop of each dilution (beginning with the weaker dilution) and 1 drop of a 2 per cent suspension of the monkey rbc are placed on a slide, mixed thoroughly with a glass rod with rounded ends (the end moving clockwise and then counter-clockwise 7 times or more, until the suspension has become homogeneous), spread over an area of about 1.5 cm. in diameter and left in a moist chamber. Two dilutions can be tested on one slide.

The slide is examined every 15 minutes for one hour with a hand lens.

A 1 in 500 dilution should show a distinct granularity with the naked eye and a 1 in 1,000 dilution a distinct granularity (made plainer with the lens).

If the serum is not up to the mark, another course of 3 or 5 injections is started the same day (anaphylaxis will not occur after an interval of 5 days only). The test is repeated 5 days after the last injection.

If the serum is up to the mark, the animal is bled from the heart 5 days after the test (10 days after the last injection), and the serum is separated and inactivated in 56°C. for one hour. The dilutions tested are: 1 in 1,000, 1 in 1,500, 1 in 2,000, 1 in 2,500 and 1 in 3,000. Four slides can be left in one moist chamber. The last dilution giving an appreciable granularity is the minimal agglutinating dose, MAD, and the next dilution (without granularity) is the sub MAD. Ten sub MAD are used for a testing dose for human rbc.

If, for instance, the last dilution giving an appreciable granularity, in one hour, be 1 in 1,500, the MAD is 1 in 1,500 and the sub MAD is 1 in 2,000. The testing dose for the human rbc is 1 in 200.

In addition to the testing dose, a dose twice as strong is used as a supporting dose which in the instance given would be 1 in 100.

(From a full-grown rabbit in Calcutta 10 to 12 c.c. of blood can be taken without killing the animal which can be used again for producing the anti-monkey-rbc serum. The first injection after an interval of more than a week is given intraperitoneally. Then the rest follows the routine.)

Whether the sub MAD is correctly selected will be shown by the reaction of the serum with known rbc (*vide infra*, superiority of the slide technique).

The clear serum to which is added 0.25 per cent tricesol is distributed in lots of 0.2 c.c. in small phials. The phials are corked and inactivated at 56°C. for one hour. They are then stored in the freezing chamber of the refrigerator. For use a bottle is taken out of the chamber and allowed to thaw slowly in the refrigerator overnight. Dilutions made from the liquefied serum for use are kept in the refrigerator. One phial lasts several days.

The serum may also be put in 1 c.c. ampoules for despatch by post.

Technique of Testing Blood with Animal Testing Serum

The suspension of rbc.—A 2 per cent suspension is used. Preferably the blood should be taken freshly in a citrate solution. Washed rbc from a fresh clot can also be used.

The slide technique.—Each slide is marked into three compartments on the obverse. On the reverse is given the distinctive number or marked along the lower border. The left-hand compartment is for the supporting dose, the middle compartment for the testing dose and the right-hand compartment for a dilution of normal rabbit serum, giving the same amount of froth as the dilution of the testing dose, thus:

1	2	3
Supporting dose.	Testing dose.	Normal rabbit serum.

All quantities are measured in standard drops. The dilutions are deposited first and

then is added the suspension. The mixing is done as usual. The results are read every 15 minutes for an hour.

A — in compartment 1 makes a — in compartment 2 doubly certain : hence the term supporting dose.

A \pm both in compartments 1 and 2, without any difference, is occasionally recorded. The granularity is really due to agencies other than anti-Rh body. Such a reaction though recorded other than — is looked upon with suspicion.

The tube technique.—Each suspension needs two 4 inches \times $\frac{1}{2}$ inch tubes, thus :

	Tube for test proper	Tube for control
Dilution of the testing dose	3 drops	Nil
Normal rabbit serum ..	Nil	3 drops
Suspension ..	3 drops	3 "

The tubes are shaken, left in an incubator at blood heat for one hour and stored in the cold for another hour (to allow the rbc to settle down). The deposit is then examined over the concave mirror of a microscope laid on its side and the results recorded thus :—

Agglutinated mass of rbc with irregular surface and edge	++
Mass of rbc with crinkly edge	+
Deposit of rbc with smooth edge which puts out a tongue on tilting the tube	—
Deposit of rbc with smooth edge which does not put out a tongue on tilting the tube	\pm

The control tube should show a smooth edge which puts out a tongue on tilting the tube.

Superiority of the slide technique.—Besides being economical the slide shows the difference in hæmagglutination much better than the tubes in the following details : (1) Size of the agglutinated masses. (2) Whether (i) centrifugal, (ii) centripetal, (iii) mixed or (iv) changing from centrifugal to centripetal by forming plaques.

These details are used in comparing two or more lots of animal testing sera on (1) sample of strongly agglutinating rbc and (2) samples of weakly agglutinating rbc. With proper adjustment of the dose all sera should give the same results (*vide supra*, correct selection of the sub MAD). Any serum showing a difference is rejected.

In the writers' opinion inferior results obtained by early Rh workers on slides were due to : (i) inaccurate measurements, (ii) insufficient mixing of the serum and the rbc, (iii) insufficient time usually allowed for reaction on slide, and (iv) difficulty of reading + and \pm results when all the rbc have deposited more or less uniformly on the slide—this will not occur if the slides are shaken every 15 minutes. Lately, workers have been using the slide technique on a large scale.

Collection of a Human Testing Serum

An isoimmunized subject.—The mother who has given birth to a baby suffering from erythroblastosis foetalis is usually (*vide infra*, Hr and group incompatibility in erythroblastosis foetalis) an Rh— subject who has become isoimmunized by her Rh+ foetus (the foetal blood escaping into the maternal circulation and immunizing the mother as the injected monkey blood immunizes a rabbit).—Her serum will agglutinate rbc of most subjects, which otherwise should not be agglutinated.

Tests for isoimmunization and suitability of a serum : 1. *When the mother belongs to group A.*—Test serum (as in grouping blood) with 3 lots of rbc A and 3 lots of rbc O. If there is hæmagglutination, exclude the intragroup reaction and subgroups of A and then suspect isoimmunization. Continue tests until several negative reactions (no hæmagglutination) are obtained. The suspicion is now confirmed. Continue further tests until the expected Rh— rate is obtained. The serum is now proved to be suitable for testing for Rh hæmogen.

2. *When the mother belongs to group B.*—Test serum with 3 lots of rbc B and 3 lots of rbc O. If there is hæmagglutination suspect isoimmunization and proceed as above.

3. *When the mother belongs to group AB.*—Test serum with 3 lots of rbc of any group. If there is hæmagglutination suspect isoimmunization and proceed as above.

4. *When the mother belongs to group O.*—Test serum with 3 lots of rbc O. If there is hæmagglutination suspect isoimmunization and proceed as above.

Intragroup and anomalous reactions, connected and unconnected with pregnancy, are known.

Use of human anti-Rh serum.—The serum unless derived from a subject AB is used for testing subjects of the same group. If its isonins can be neutralized (by substances A and B, obtained from saliva of secretors) it can be used for testing subjects of all groups. It can be stored liquid or freeze-dried.

The serum is used undiluted, as in grouping blood. The results obtained are clear-cut ++, + and — (no \pm). Both slides and test tubes may be used.

Several types of Rh hæmogen.—In Europe and America about 2 per cent of the populations though negative by animal serum and a standard human serum (which gives the same Rh— percentage) is positive by special (and rare) human testing sera. The hæmogens in their rbc are qualitatively different from the standard Rh hæmogen. Without going into details of these types which are yet in a fluid state regarding definition, the important conclusion can be stated clearly: A subject Rh— by animal serum and human serum may be really Rh+ of a different type. Do not, therefore, recommend transfusion of whole blood for an Rh— subject unless : (1) All testing sera are

available. (2) The serum of the recipient who is a mother can be used for testing the donor's rbc *carefully*. (3) The serum of the recipient receiving a second or subsequent transfusion can be used for testing the donor's rbc *carefully*. (4) A biological test can be performed. To perform this test (i) take 10 c.c. of the recipient's blood and divide into two lots in (a) a dry test tube and (b) a test tube containing 1 c.c. of 3.8 per cent sodium citrate, (ii) allow the blood in (a) to clot and centrifuge (b), (iii) give intravenously 50 c.c. of the proposed donor's citrated blood as a sample, (iv) after one hour draw 10 c.c. of the recipient's blood and distribute into 2 test tubes, dry and wet, as before, (v) allow the blood in the dry tube to clot and centrifuge the wet tube as before, and (vi) compare the colours of the supernatant fluids of the wet tubes and the colours of the serum in the dry tubes. Absence of colour denotes absence of hæmolysis. The wet tubes guide against a traumatic hæmolysis of the rbc which might occur in the dry tubes.

The biological test even if positive (the second sample of the serum showing a tinge of hæmolysis) will not do the recipient any appreciable harm. It may however damage further a foetus suffering from erythroblastosis foetalis, by raising the titre in the mother's serum. An unmarried Rh— female may be sensitized in advance of an incompatible pregnancy (*vide infra*).

Every Rh— mother of an Rh+ foetus is not isoimmunized.—The escape of the foetal blood into the maternal circulation may not take place. The stimulus, even after an escape of blood, may not be strong enough. Usually an Rh— mother can have two healthy Rh+ babies. Later, the repeated stimulus succeeds in producing the antibody.

Every isoimmunized Rh— mother of an Rh+ foetus does not produce an effective anti-Rh body.—Some mothers instead of producing a hæmagglutinin produce a hæmagglutinoid or a blocking body. Their serum does not agglutinate but so affects the Rh+ rbc that later even an effective antiserum cannot agglutinate them.

An Rh— wife of an Rh+ husband does not always carry an Rh+ foetus.—The reason is genetic. If the husband is heterozygous his gametocytes contains both an Rh+, Rh, and an Rh—, rh character. Some gametes will carry Rh and other rh. The gametes of the wife will of course carry only rh. The zygote resulting from gametes carrying rh will develop into an Rh— foetus, in spite of the fact that the husband is Rh+.

A homozygous husband on the other hand produces gametes containing only Rh character.

DETERMINATION OF Rh HOMOZYGOUS/HETEROZYGOUS STATE

Occasionally an Rh+ mother gives birth to a baby suffering from erythroblastosis foetalis.

She provides an anti-Hr serum or St. serum. It contains an antibody against the Hr hæmogen which is associated with character rh.

The serum agglutinates the rbc of all Rh— subjects and all heterozygous Rh+ subjects.

The tests are performed as in the determination of groups, types or Rh+ /— state.

DETERMINATION OF OTHER CAUSES OF ERYTHROBLASTOSIS FOETALIS

Occasionally incompatibility of blood groups gives rise to erythroblastosis foetalis. The titre of the isonin in the mother's serum for the isogen in the rbc of the foetus is found to be very high (of the order of a thousand). After delivery the titre falls.

Other incompatibilities, M, N, and P, etc., have not attracted attention so far. They may also operate. *To be continued.*

FURTHER OBSERVATIONS ON CASES OF ASTHMA AND BRONCHITIS ASSOCIATED WITH HIGH EOSINOPHILIA AND WITH MITES IN THE SPUTUM

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It is now becoming apparent that in Ceylon an appreciable, possibly even a high, proportion of cases of asthma and bronchitis is of the type lately recognized by Frimodt-Møller and Barton (1940), Weingarten (1943) and others as constituting a definite group or condition characterized, at least in the later stages, by high or massive eosinophilia and usually specific radiological appearances of the lungs. In a recent paper (Carter and D'Abbrera, 1946) an account of the investigations carried out on 25 Ceylonese patients, all of whom were suffering from or had recently suffered from respiratory disorders and showed an initial eosinophilia of 3,000 per c.mm. or over was given. More than 200 samples of sputum were examined and at one time or another mites of the types commonly present in stored products, dust and debris were found in all but one patient. Considerations of the evidence obtained in these and in previous investigations (Carter, Wedd and D'Abbrera, 1944) led us to believe that the mites found in the sputum were derived from the respiratory tract and to advance the view that they were probably a factor in the ætiology of the condition. This view was supported by the work of Soysa and Jayawardena (1945).

In this note observations on six additional cases which present points of special interest are given.

Case 1.—Male, 52 years; occupation, clerk. History of bronchial asthma of 11 months' duration when seen on 24th August, 1944; first asthmatic attack on 21st October, 1943, after several weeks of persistent bronchitis. Treated intramuscularly with bismuth

('Bismostab') and subsequently, after an observation period of 49 days during which bronchitis with intermittent attacks of asthma continued, with 'carbarsone'. Details of the treatment and of the results of examination of the blood and sputum are given in table I. The asthmatic attacks ceased on the fourth day of arsenical treatment and the bronchitis on the tenth day after completion of this treatment.

were found in the patient's sputum. But from the data given above it will be seen that treatment with bismuth had little effect either upon the clinical condition of the patient or on the blood. The absolute figures for total leucocytes and for eosinophils had decreased by the end

TABLE I

Case 1

Date	Treatment	Leucocytes, per c.mm.	Eosinophils,		Sputum (24-hour samples)
			per c.mm.	per cent	
24-8-44	..	41,000	28,250	69.0	T.B. negative, spirochaetes +.
7-9-44	3 mites.
2 to 16-10-44	Bismuth 1 c.cm. on 2, 6, 9 and 13-10-44.	6 mites in 5 out of 6 samples.
18-10-44	..	40,200	31,195	77.5	1 mite.
10-11-44	..	34,000	25,190	74.2	Not examined.
16-11-44	..	31,200	20,405	65.5	Do.
17 to 27-11-44	4 mites in 3 out of 6 samples.
30-11-44	..	28,400	19,590	69.0	Not examined.
2 to 8-12-44	Carbarsone 0.5 gramme on first 3 days, 0.25 gramme on remainder.	1 mite in 2 samples.
9 to 15-12-44	2 mites in one of 3 samples.
18-12-44	..	10,200	4,080	40.0	No sputum obtainable for examination.
11-1-44	..	8,600	1,720	20.0	
25-1-45	..	10,600	1,490	14.0	
6-2-45	..	8,000	1,300	16.2	

In this case, bismuth was administered as a therapeutic test with a view to ascertaining whether the condition was of spirochaetal origin. Bronchial infections attributed to spirochaetes have been reported from Ceylon by Castellani (1906) and from America by Bloedorn and Houghton (1921). The first-named author found large numbers of actively motile spirochaetes (which he named *Spiroschaudinna bronchialis*) but no tubercle bacilli in the sputum of two patients who had suffered from recurrent hæmoptysis over periods of several months. The American authors reported a similar case in which the patient made a complete recovery following intravenous administration of neoparsphenamine. In the latter case the results of blood examinations were mentioned, but no specific reference was made to the eosinophils which presumably, therefore, were not in excess of the normal. Wenyon (1926), however, considered that there was little evidence that the spirochaetes which occur in the bronchi were in any way more pathogenic than those which are found so commonly in the mouth. The differentiation of pathogenic and non-pathogenic spirochaetes on morphological characters being a matter of considerable difficulty, and bismuth being a recognized spirochaetocide, it was thought that a therapeutic test with a substance of this nature other than organic arsenic might offer results of interest in relation to the condition under discussion, as both spirochaetes and mites

of the observation period from 30,000 to 20,000, but were still very high, and the percentage of eosinophils was approximately the same as that before the treatment commenced. The results in this particular case, therefore, would not seem to lend support to the contention that the spirochaetes present were responsible for the condition.

Case 2.—Male, 37 years; occupation, radio inspector. History of asthma of 3 years' duration when first seen on 21st August, 1944. Treated intramuscularly with antimony ('anthiomaline')—6 c.cm. over a period of 8 days) and later—after one week as the asthma was not controlled and was severe—with carbarsone. During the latter treatment the asthmatic attacks ceased and the patient subsequently remained free for a period of 7 months when a sharp attack followed by three days of bronchitis occurred. A second course of carbarsone was then administered. No sputum was produced during the relapse. Details of the treatments given and of the results of examination of the blood and sputum are given in table II. In all 20 samples of sputum were examined and 21 mites of various types (chiefly Tarsonemids and Tyroglyphids) were recovered from 13 of the samples. Prior to treatment five samples of sputum were examined and two mites were found in one of these. Three mites were found in three samples examined during treatment with anthiomaline, 11 mites in five out of six samples during treatment with carbarsone, and 5 mites in four out of six samples examined in the period of ten days following carbarsone treatment during which sputum was still being produced.

Antimony in the form of anthiomaline appeared to have no effect either upon the clinical or blood conditions of this case.

TABLE II
Case 2

Date	Treatment	Leucocytes, per c.mm.	Eosinophils,		Sputum (24-hour samples)
			per c.mm.	per cent	
21-8-44	..	28,000	20,540	73.4	T.B. negative.
22 to	2 mites in one of 5 samples.
26-8-44
29-8-44	Anthiomaline 2 c.cm.	Negative.
30-8-44	..	28,200	19,176	68.2	1 mite present.
1-9-44	Anthiomaline 2 c.cm.	Not examined.
2-9-44	..	26,000	20,150	77.3	1 mite present.
4-9-44	Do.
5-9-44	Anthiomaline 2 c.cm.	Not examined.
11-9-44	..	26,600	17,449	65.6	Do.
12 to	Carbarsone 0.5 gramme on	11 mites found in 5 out of
19-9-44	first 4 days, 0.25 gramme on	6 samples examined.
	remainder.
21 to	5 mites found in 4 out of
30-9-44	6 samples examined.
3-10-44	..	10,000	3,370	33.7	..
17-10-44	..	7,200	1,476	20.5	..
19-1-45	..	10,800	2,030	18.9	..
23-3-45	..	6,400	1,290	20.2	..
20-4-45	(Relapse—one sharp attack of asthma)	No sputum available.
21-4-45	..	10,000	1,360	13.6	..
22 to	Carbarsone 2.5 grammes
28-4-45
11-5-45	..	5,600	492	8.8	..

Antimony was used as a therapeutic test to eliminate the possibility of an organism belonging to the genus *Leishmania* being responsible for the disease.

Case 3.—Female, 35 years, wife of case 2. History of spasmodic bronchitis—no asthma—of 3½ years' duration when seen on 23rd January, 1944, when she was in the sixth month of her first pregnancy. Two blood examinations made on 23rd November, 1944, and 30th November, 1944, showed respectively total leucocytes 34,000 and 41,000 per c.mm. with eosinophils 18,900 (55.6 per cent) and 24,600 (60 per cent) per c.mm. Eight samples of sputum examined prior to and during treatment revealed nine mites in five of the samples. Treatment with carbarsone was commenced on 1st December, 1944, 2.5 grammes being administered over a period of eight days. The bronchial symptoms had disappeared by the time treatment was completed and pregnancy progressed to term, the child being born on 6th April, 1945. The puerperium was uneventful.

So far as I am aware this is the first record of the condition ('tropical eosinophilia') occurring in husband and wife. It would appear also that in both the clinical symptoms developed about the same time—in the husband asthma in May 1941, and in the wife spasmodic bronchitis in April 1941. Similar types of mites were present in the sputum of both patients. Treatment with 'carbarsone' did not affect pregnancy and relieved the patient considerably ensuring rest and sleep and freedom from cough at night.

Case 4.—Female, 23 years, married. History of bronchitis and asthma of six months' duration when seen on 25th June, 1944, when she was in the seventh month of her first pregnancy. Total leucocytes 30,000 per c.mm. with eosinophils 15,300 (51 per cent) per c.mm. Sputum—two mites found in one sample examined on 26th June, 1944. No treatment was given

and the patient was delivered of a healthy child on 23rd August, 1944. Labour was however difficult owing to exhaustion from violent bouts of coughing. On 25th August, 1944, the blood of both the mother and child was examined. The counts obtained were as follows: mother—total leucocytes 40,000 per c.mm. with eosinophils 12,400 (31 per cent) per c.mm.; child—total leucocytes 11,400 per c.mm. with eosinophils 450 (4 per cent) per c.mm., neutrophils 6,270 (55 per cent) per c.mm. and lymphocytes 4,670 (41 per cent) per c.mm. The patient had a febrile puerperium which lasted 30 days. She was treated with sulphonamides. The mother's blood was again examined on 2nd May, 1945, with the following result: total leucocytes 10,200 per c.mm., eosinophils 2,350 (23 per cent) per c.mm. On 20th September, 1945, she sought treatment again as the cough which had never left her became more troublesome. Blood examinations revealed total leucocytes 35,000 with 26,075 eosinophils (74.5 per cent) per c.mm. She has now consented to take a course of arsenic treatment.

This case is of interest owing to the effect the syndrome had on labour and the puerperium. The patient was not prepared to undergo a course of arsenic treatment owing to the fear of an exacerbation of the symptoms coming on and provoking the onset of a premature labour. On the other hand, case 3, also a primipara, profited from the early administration of arsenic.

Case 5.—Male, 8 years, school boy. History of severe and frequent attacks of asthma of 4 months' duration when seen on 8th August, 1944. He also had evening temperature, loss of weight, anorexia and was confined to bed. Total leucocytes 60,000 with 42,000 (70 per cent) eosinophils per c.mm. X-ray showed 'eosinophil lung'. Two samples of sputum, out of six examined before treatment, had a total of two mites, whilst from five samples during treatment, all of which were positive, a total of 14 were collected. Two samples after treatment were negative. The mites obtained

were chiefly Tarsonemids and Tyroglyphids. Treated with carbarsone (B.&W.) combined with vitamin C over a period of five days, treatment commencing on 22nd August, 1944. On the 26th the patient became very ill, temperature rose to 103°F., status asthmaticus supervened which lasted two days. The arsenical was stopped after 0.75 gramme had been administered and Dagenan (M.&B. 693) substituted. Temperature dropped, asthmatic attacks ceased and he made a quick recovery. A second course of the arsenical (1.0 gramme) was administered ten days later. Blood examination on 23rd September, 1945, revealed total leucocytes 8,000 with 1,080 (13.5 per cent) eosinophils per c.mm.

Considering the fact that secondary bacterial organisms are always present in the expectoration of these patients the action of the sulphonamide in controlling the exacerbation (*vide* also case 18, Carter and D'Abrera, 1946) is probably due to its remarkable potency as a bactericidal agent. Administered solely for controlling the primary condition (case 3, Carter, Wedd and D'Abrera, 1944, and case 1, Carter and D'Abrera, 1946) it does not seem to have effected a cure although Lal (1945) thinks otherwise. Several workers have controlled the exacerbation by continuing the arsenical treatment (case 17, Carter and D'Abrera, 1946) but the patients were undoubtedly subjected to very grave risks as the status asthmaticus was prolonged. This tardy effect when compared with the sulphonamide, at controlling the secondary infection, is probably due to the insufficient concentration of the arsenical in the blood; to increase which would not be justified (Colebrook, 1928) without risking the destruction of large numbers of leucocytes.

Case 6.—Male, 21 years, bank clerk (same as case 9—Carter and D'Abrera, 1946). The patient originally had a total leucocyte count of 36,000 with 26,460 (73.5 per cent) eosinophils per c.mm. Sputum was positive to mites and after two courses of treatment with stovarsol he remained free from asthma for eleven months. Six months after treatment, he had a total leucocyte count of 10,300 with 1,340 (13 per cent) eosinophils per c.mm. On 12th February, 1945, the patient sought treatment for a relapse of the asthma, which he said came on following a period of three weeks' bronchitis after contracting a common cold. Blood examination revealed a total leucocyte count of 23,800 with 13,450 (56.5 per cent) eosinophils per c.mm. A course of leucarsone (M.&B.) 2.5 grammes was administered commencing on 20th March, 1945. Two months later his blood examination revealed a total leucocyte count of 6,400 with 475 (7.4 per cent) eosinophils per c.mm. Cough was not productive, only two samples being obtained with difficulty, both of which were negative for mites.

This is the second case, the other being case 2, which sought treatment for a relapse. Both cases on their initial visits had productive coughs, and mites were recovered from the sputum. Both continued to live under the same environmental condition, as during their initial attacks. It is probable that the relapses were due to inhalation of a few mites by individuals already sensitized to the specific allergen.

Summary

Six cases of tropical eosinophilia presenting points of special interest are recorded. The

sputum of all cases was positive to mites.

1. Two cases were employed for determining the therapeutic effect of bismuth and antimony on the course of the disease. The sputum and blood records are tabulated. As the drugs used had no therapeutic value, organic arsenicals were later administered to obtain a clinical cure.

2. Two cases complicating pregnancy are recorded. In the treated case the labour was easy and the puerperium was uneventful, whilst in the untreated case the patient had a difficult labour owing to exhaustion from violent bouts of coughing, the puerperium being also febrile. The blood condition was not conveyed from the mother to the infant.

3. Two cases with relapses are recorded.

4. The occurrence of the malady in both husband and wife is recorded for the first time, the husband being in the 'asthmatic phase' and the wife in the 'bronchitic phase' of the syndrome.

5. The action of sulphonamides in controlling the exacerbation resulting from the administration of arsenicals is discussed.

Acknowledgment.—I am indebted to Mr. H. F. Carter, Medical Entomologist, Ceylon, for his collaboration in the entomological aspects of these investigations and for his help and advice in the preparation of this paper.

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CYST IN THE VITREOUS AND POSTERIOR POLAR CATARACT IN RETINITIS PIGMENTOSA

By G. FALCONE, M.D. (Rome)

A cyst in the vitreous is a very rare occurrence and the few observations reported in the literature do not always give a full explanation about their origin.

Sometimes the presence of cysts in the vitreous occurs in a diseased eye and in pigmentary degeneration of the retina cysts have been

found (Litinsky, 1931; Perera, 1936); sometimes they appear to be anomalies of development, as remains of the hyaloid system (Koller 1901); sometimes apparently congenital cysts may be the result of a disease occurred during the foetal life. The lack of anatomico-pathological examinations has not yet established the nature of these formations which generally are symptomless. Most of them, whatever their origin may be, are transparent and more or less freely floating in the vitreous.

The posterior polar cataract is generally considered as a residual of the hyaloid canal and therefore belongs to the congenital anomalies; but it may be also a complicated cataract due to diseases of the retina, or of the choroid, during the intra- or extra-uterine life.

The aetiology of the primary pigmentary degeneration of the retina, usually but improperly called retinitis pigmentosa, is still obscure in many respects: the characteristics of heredity, the association with mono- or poly-glandular dystrophic syndromes, and the slow and progressive chronic course are in favour of the theory that the condition is an abiotrophic process. Other theories, based on anatomical and physiological data, consider the disease as a result of the sclerosis of the choroidal vessels, sometimes hereditary and abiotrophic in character (Sorsby 1939) with consequent disappearance of the choriocapillaries. Toxic causes, liver deficiency and avitaminosis have been also associated with pigmentary degeneration of the retina. Pathologically the degeneration of the neuro-epithelium affects principally the rods; an attenuation of the retinal vessels and a waxy-yellowish discoloration of the disc follow the pigmentary changes. The night-blindness is admittedly connected with the primary affection of the rods.

A posterior polar cataract of the complicated type is found in the advanced stage of the pigmentary degeneration of the retina; it is considered as the effect of the malnutrition of the lens due to accumulation in the vitreous of toxic products originated from the retinal and choroidal changes.

A case of primary pigmentary degeneration of the retina associated with posterior polar cataract in B.E. and a cyst in the posterior segment of the vitreous in L.E. is reported.

A male patient, aged 27 years. For some years he complained of progressive night-blindness. No important diseases in the previous history. Systemic examination showed quite good general condition; routine laboratory investigations were negative.

Ophthalmic examination:—

Vision B.E. = 6/9 no improvement with lenses.

Field of vision B.E.: Ring scotoma.

Media B.E.: Opacity on the posterior pole of the lens, like a small cone with the apex penetrating in the vitreous.

Fundus B.E.: Optic disc of waxy-yellowish colour, with ill-defined edges. Thin, thread-like vessels. The whole fundus had a yellowish-pink aspect with characteristic and scattered deposits of pigment of a spidery shape, resembling magnified bone corpuscles, mainly present in the equatorial zone.

In the L.E. on the nasal side of the fundus about $\frac{1}{2}$ D.D. medially to the disc a non-transparent cystic formation was seen: it was of oval shape with smooth surface, greenish-grey in colour; its greater diameter was longitudinal and the slenderer upper pole was apparently more close to the retinal surface; its dimension was $\frac{1}{2}$ D.D. The cyst was floating in the vitreous with very limited movements.

The association of the pigmentary degeneration of the retina with bilateral posterior polar cataract, and with a cyst in the vitreous gives rise to two different interpretations:

1. The cyst may be considered as an embryonic remain of the hyaloid circulation, and the polar posterior cataract may be attributed to the same origin.

2. The cyst and the cataract may result from the altered biochemistry of the vitreous and of the posterior capsule of the lens due to the changes in the retina and choroid.

The first hypothesis seems more probable but, whatever may be the connections between these various conditions, it is interesting to note in this case the association of a very likely congenital anomaly with a dystrophy which from its abiotrophic nature may also be congenital.

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SUICIDAL POISONING IN CALCUTTA

By KABIR HOSSAIN, M.B., D.T.M.

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SUICIDE or 'self-murder', is regarded by the law as murder, a murder committed by a person on himself or herself (*felo-de-se* or felony committed on one's self). The verdict usually given by the coroner and other competent authorities in such cases is 'Death is due to suicide, whilst temporarily insane'. This expression is regarded as a charitable addition to relieve the suicide and his family from the stigma attaching to this act.

Any person aiding or abetting suicide is also guilty of the charge of murder. An attempt to commit suicide is punishable under the law in India though in a less degree than an attempt to commit murder—a common misdemeanour.

Modes of suicide vary considerably according to local conditions, such as the presence of a river or lake, habits of the people, accessibility of weapons or fire-arms, poisons, etc. In India, the methods of self-destruction chiefly employed are: (1) drowning, (2) hanging, (3) poisoning, (4) burning, (5) shooting, (6) starving, (7) placing or throwing oneself on the railway lines, (8) falling or jumping from a precipice,

and (9) by inflicting wounds on the body such as stabbing on the region of the heart or cutting the throat.

Chiefly poisons are used as a means of suicide and certain poisons are used specially in certain areas and by certain classes. The intending suicide seems to be under the impression that all poisons kill without causing suffering.

Suicide in Calcutta

At the Calcutta Police Morgue, 2,139 post-mortem examinations were held on cadavers sent by the police from 12 police stations in Calcutta proper, during the period of four years (1942-45). Out of these 115 cases were found to have died from poisoning—as was determined from post-mortem findings and subsequent chemical examination of viscera. A glimpse of the year-to-year analysis of cases of poisoning detected at the Calcutta Police Morgue (recorded in table I) will give an idea as to the nature of poison used in Calcutta, its percentage and incidence.

TABLE II
Suicidal poisons, used in Calcutta, during 1942-45

Name of poison	Definitely suicidal	Probably suicidal	Total	Percentage
1. Acid carbolic ..	1	1	2	2.7
2. " nitric ..	1	0	1	1.4
3. " oxalic ..	0	1	1	1.4
4. " sulphuric ..	2	2	4	5.5
5. Arsenic ..	1	0	1	1.4
6. Barbiturate (alonal) ..	0	1	1	1.4
7. <i>Calotropis gigantea</i> (madar or akanda).	1	1	2	2.7
8. Copper sulphate ..	4	1	5	6.8
9. Hydrocyanic acid and cyanides.	11	1	12	16.4
10. Morphine ..	1	0	1	1.4
11. Opium ..	23	19	42	57.5
12. Zinc chloride ..	1	0	1	1.4
	46	27	73	

TABLE I

Cases of poisoning detected at the Calcutta Police Morgue, and confirmed by the Chemical Examiner to the Government of Bengal during the period 1942-45

Name of poison	1942	1943	1944	1945	Total	Percentage
1. Acid carbolic ..	1	0	1	0	2	1.7
2. " nitric ..	0	1	1	0	2	1.7
3. " oxalic ..	1	0	0	0	1	0.87
4. " sulphuric ..	2	0	2	2	6	5.2
5. Aconite ..	1	0	0	1	2	1.7
6. Alcohol ..	2	6	3	3	14	12.2
7. Arsenic ..	0	0	1	1	2	1.7
8. Atropine (as datura) ..	1	2	1	2	6	5.2
9. Barbiturate ..	1	0	1	0	2	1.7
10. Carbon dioxide and monoxide.	0	0	2	0	2	1.7
11. Carbon monoxide ..	1	0	1	0	2	1.7
12. <i>Calotropis gigantea</i> (madar or akanda).	0	1	0	1	2	1.7
13. <i>Cannabis sativa</i> (bhang) ..	0	1	0	0	1	0.87
14. Copper sulphate ..	1	1	1	2	5	4.3
15. Cresol ..	0	0	1	0	1	0.87
16. Hydrocyanic acid and cyanides.	2	4	3	4	13	11.3
17. Morphine ..	0	0	1	0	1	0.87
18. Opium ..	12	11	11	14	48	41.7
19. Phosphorus ..	0	1	0	0	1	0.87
20. Scorpion bite ..	1	0	0	0	1	0.87
21. Zinc chloride ..	0	0	0	1	1	0.87
	26	28	30	31	115	

Coroner's inquest was held on all these cases at the Calcutta Coroner's Court. Out of 115 cases of poisoning, 73 were found suicidal (46 definitely suicidal and 27 probably suicidal), only one was homicidal and the remaining 41 were either accidental or probably accidental.

An idea about the nature of poison used for suicidal purpose in this series of cases may be obtained from table II.

Suicidal poisoning with relation to sex

Taking all the methods of suicide together into consideration in the literature, it is found that commission of suicide is more common among females than among males. But in the Calcutta series of cases of suicidal poisoning, it is two and a half times more common among males than among females as can be seen from table III.

TABLE III
Suicidal poisoning tabulated according to sex

Sex	Definitely suicidal	Probably suicidal	Total	Percentage
Male ..	30	22	52	71.2
Female ..	16	5	21	28.8
	46	27	73	

Another peculiar thing to note in this connection is that in some of the females who committed suicide, evidence of menstruation at the time of death was noticed on examination of their genital organs. This corroborates the prevalent belief that during the menstrual period, certain females, specially those of neurotic type, get some disturbances in their mental equilibrium which make them inclined to commit suicide.

Suicidal poisoning with relation to community

Suicide is not at all common among the Muslim, Indian Christian and Anglo-Indian communities. But it is prevalent amongst the Hindu community. The reason is not properly understood as suicide is condemned by all religions. This communal differentiation is shown in table IV.

TABLE IV
Suicidal poisoning tabulated according to community

Community	Definitely suicidal	Probably suicidal	Total	Percentage
Hindu	45	25	70	95.9
Muslim	1	0	1	1.4
Indian Christian.	1	0	1	1.4
Anglo-Indian.	1	0	1	1.4
	48	25	73	

Suicidal poisoning with relationship to age group

Taking all the modes of suicide together into consideration, suicide is more common among

TABLE V
Suicidal poisoning tabulated according to age groups

Age group, years	Definitely suicidal	Probably suicidal	Total	Percentage
Up to 10	0.0
11-20 ..	9	5	14	19.2
21-30 ..	26	11	37	50.7
31-40 ..	7	6	13	17.8
41-50 ..	3	4	7	9.6
51-60 ..	1	1	2	2.7

adults usually between the ages of 16 and 50. It is very rare among children and old people above 50 years. In the series of cases of death from suicidal poisoning, highest incidence (50.7 per cent) was seen in the years 21 to 30, no case amongst children before 10 years and the least (2.7 per cent) in people above 50 years. Table V gives the incidence of suicidal poisoning in different age groups.

The poison selected for committing suicide

1. *Opium and morphine.*—Opium is the drug of choice. This drug is easily obtainable everywhere in India and death occurs easily without any physical suffering, opium poisoning is fairly common in the Punjab and in Bengal. Nearly 35 to 40 per cent cases of fatal poisoning in Bengal investigated by the Chemical Examiner were due to opium; in the Punjab the percentage of such cases is found to be 40 to 42 per cent. In this series 57.5 per cent cases of fatal poisoning were due to opium. Suicide by morphine is comparatively rare in India. Table II will show that there was only one case of suicide by morphine as against 42 cases by opium.

It is stated that suicides usually mix opium with mustard oil or asafoetida in the belief that these substances increase its absorptive power but there is no foundation about this belief. However, it is true that mustard oil makes it difficult to be eliminated even by washing out the stomach. It is also believed that alcohol hastens the action of opium, but it does not do so in all cases. Curiously enough mustard oil or asafoetida was not found mixed with opium in any of this series of cases, but in 5 cases alcohol was found with opium by the Chemical Examiner.

2. *Hydrocyanic acid and cyanides.*—This group occupies the second place in the list of suicidal poisons (16.4 per cent). Cyanide poisoning is common in England and other European countries. Of late years, however in India too, it has been more commonly used than before for committing suicide by young educated persons especially in big towns and cities. This group of poisons is preferred now for their swift and sure action. Cases are reported where the victims expire even before they put the poison-cups on the table.

Hydrocyanic acid is a very powerful poison but it is not accessible to all. Cyanides of sodium and potassium are also highly poisonous but are at the same time easily accessible on account of their extensive use in various industries. The toxic action of potassium cyanide depends largely upon the hydrochloric acid of the stomach. It is reported that Rasputin was saved from sure death from cyanide poisoning, owing to his having alcoholic gastritis wherein achlorhydria is a feature.

Alkali cyanides, if exposed to air, are readily converted into carbonates by the action of CO₂ and moisture of air. Old samples of these

cyanides may, therefore, contain quite a considerable amount of carbonates and only a small amount of cyanides. Hence suicidal attempts by taking large doses of such cyanides have known to be unsuccessful.

3. *Copper sulphate*.—Fatal cases of copper poisoning frequently occur in Bengal and also in other parts of India. They are mostly suicidal or accidental and rarely homicidal. Sometimes copper sulphate is also taken as an abortifacient drug but the woman dies usually of copper poisoning 3 or 4 days after the miscarriage. Copper sulphate is selected by females generally for committing suicide. All the 5 cases of copper sulphate poisoning in this series were females.

4. *Calotropis gigantea* or *madar*.—*Calotropis* is known in this country from ancient times for its medicinal and other properties. It is known as 'akanda' in Bengal. Madar-juice is occasionally used for the purpose of suicide, but it is more commonly used by mouth or locally as a paste to be placed at one end of an abortion-stick for procuring abortion. The small stems are often used as abortion-sticks which are inserted into the os uteri. Sometimes young females develop amenorrhœa due to other causes, but they fear that they have conceived. They take this poison with an intent to cause abortion.

History of one case of poisoning from madar in this series is that the deceased, a Hindu married woman aged about 25 years, had no child. She left her husband's protection due to ill-treatment and lived as a mistress elsewhere. She complained of pain in the abdomen associated with fever and expired later on. On autopsy, uterine cavity was found to contain a little blood and right ovary a blood clot. Report of the Chemical Examiner showed the presence of *Calotropis gigantea* but pathological section showed no sign of conception.

5. *Sulphuric acid* is very largely used commercially in several trades. Hence it is easily obtainable and may sometimes be taken for suicidal purposes. Most cases of sulphuric acid poisoning in the East are suicidal especially among adult women. Three out of 4 cases of sulphuric acid poisoning in this series were females.

6. *Nitric acid* is very largely employed in art and manufacture. Cases of poisoning are not very common. In this series there is only one such case of poisoning.

7. *Oxalic acid*.—During recent years, cases of suicide by oxalic acid poisoning, although very few, have occurred in India, due to its increased use as a remover of stains on clothes and the ease with which it can be obtained at a druggist's shop.

8. *Carbolic acid*.—Being easily procurable it is one of the common poisons used for suicidal purpose. Two such cases were found in this series.

9. *Arsenic*.—The fatal cases of arsenic poisoning are mostly homicidal. This is used

occasionally for suicidal purposes, but owing to much pain caused by its ingestion, suicides resort to this poison much less frequently than to opium. The only case in this series was a Hindu female aged about 20 years. She gave a statement that she had a quarrel with her husband and in fury took 'rough on rat' a poison containing arsenic.

10. *Barbiturate* (alonal) is sometimes taken for suicidal purpose. The only case in our series, an elderly Anglo-Indian female aged about 50 years, was found dead in her room, the door being bolted from inside. On opening the room, one phial of carbolic acid and 5 phials of alonal were found.

11. *Zinc chloride*.—Deceased, a Hindu male aged about 23 years, a dealer in vegetables, made a statement that he was implicated in a theft case, took the poison and went to Mayo Hospital.

Poisoning by zinc salts is very rare. Zinc chloride has been used suicidally, but rarely for homicidal purposes.

Motives of suicide

Motives for committing suicide are determined from personal statements of the victims before death, from letters left by some of them or from coroner's inquest into the causes of death. But in the majority of the cases under review, no cause has been found even after thorough investigation of these cases. In some of the cases where letters have been left, no clue has been found except the information that nobody was responsible for the victim's death, or that he was leaving his relatives for ever, or that he did not like to disclose his motive for certain reasons.

The motives that were found fall under the following heads :—

1. *Domestic troubles and worries*.—11 cases.

(a) *Quarrel between the wife and the husband or his relatives* (9 cases).—In one of our cases, both husband and wife took opium due to some quarrel in the family; the husband died, but the wife survived in the hospital. In another case, the husband rebuked his wife for not doing the household work properly—this led her to commit suicide; in still another case, wife left husband's protection due to ill-treatment and subsequently committed suicide.

(b) *Quarrel with other people* (2 cases).—In one of our cases an unmarried girl aged about 16 years committed suicide by taking strong nitric acid after a quarrel with her cousin. In another case the victim had a quarrel with his master who ill-treated him for a long time.

2. *Poverty and financial difficulties* (5 cases).—In one of our cases, the victim lost money at the races and was indebted, so he committed suicide by taking hydrocyanic acid. Two others were unemployed, and still another, being driven away by his master for some skin disease, could not get any other job and the fifth one, a homeless person, was suffering from

fever. For all these financial difficulties they committed suicide.

3. *Remorse and shame* (2 cases).—Both the cases have got the same story; they were prosecuted in the Magistrates' Courts on charges of theft and for this they put an end to their lives.

4. *Incurable and painful disease* (5 cases).—One of this series of cases was suffering from paralysis for a long time and had hysteric fits off and on; another was suffering from bubo; third one from leucoderma and the remaining two from chronic fevers.

N.B.—In 15 cases of this series, letters or pocket books were left intimating that they died of their own accord, but they did not disclose

their reasons for the same. In 34 cases, no causes of suicide could be determined. They were diagnosed as cases of suicide from information supplied by relatives and neighbours of the victims and by coroner's inquest.

ERRATUM

SEROLOGICAL TECHNIQUE

By S. D. S. GREVAL

and

A. B. ROY CHOWDHURY

Page 355, column 1, paragraph 4. Instead of 'Serum o comes from sub-group AB' read 'Serum o comes from group AB'.

A Mirror of Hospital Practice

A CASE OF CARCINOMA OF THE COLON WITH AMÆBIC INFECTION

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.),
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and

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IN the diagnosis of tropical diseases the laboratory findings are often of greater importance than in that of non-tropical diseases, but great care must be taken that one's clinical judgment is not outweighed by laboratory findings which may be as misleading in some cases as they may be useful in others. In this connection, the following case report will be of interest.

Case report

A man, aged 60 years, was admitted to the Carmichael Hospital for Tropical Diseases on 1st April, 1946, for dysentery. The history was that he was not keeping well for the past six months during which he had been suffering from 'dyspepsia' (constipation and flatulence being the main symptoms) with occasional bouts of fever, and had lost about four stones in weight. The dysenteric symptoms—frequent loose motions with passage of mucus and occasionally blood—were of six weeks' duration. He had been given a course of emetine injections as well as sulphaguanidine but with little or no effect.

On admission he appeared prostrated. The liver was enlarged one inch below the costal margin with normal consistency. A small ill-defined somewhat irregular mass was palpable in the left hypochondrium which could be easily pushed under the costal margin like a palpable spleen. The abdomen was soft, and there was no tenderness. Digital examination of the rectum showed no abnormality.

Laboratory findings.—The blood examination showed a white cell count of 9,100 per c.mm. The red cells were 4.2 million per c.mm. and hæmoglobin was 8.8 gm. (64 per cent). Stools: *E. histolytica* trophozoites were

found once in a serial examination for four consecutive days. The test for occult blood was positive. Gastric analysis showed a low acid curve.

X-ray examination.—A barium meal series were taken and the radiologist's opinion was 'colitis and appendicitis'. But there were certain other peculiarities which could be distinguished: The ten-hour picture (see figure 1, plate XXIV) showed a distended transverse colon with horizontal fluid level of the meal. The 24-hour picture (see figure 2, plate XXIV) revealed a segment of 'defective filling' beyond the distended transverse colon while the meal had passed distal to this segment into the large gut of more or less normal calibre. After 48 hours an irregular residual shadow of the meal was seen held up in the segment where there was the 'filling defect' (see figure 3, plate XXIV).

Diagnosis.—Considering the age of the patient, the history of the case, the clinical findings and the unusual radiological findings, we suspected a neoplastic condition of the transverse colon and transferred the patient to the Medical College Hospital where he was operated on by Major Andreasen. The tumour was found to be cancer involving a segment of the transverse colon and was adherent to the stomach wall. It was removed along with a portion of the stomach. Histologically the tumour was found to be adenocarcinoma of the colon.

The patient died of congestive cardiac failure a few days after the operation.

Discussion.—The case is of considerable interest as it presented the combined features of amœbic infection and cancer of the large bowel. In the practice of tropical medicine it is common to encounter multiple infections in the same patient, and it is therefore not always safe to attempt and trace all the signs and symptoms to a single infection or pathological process. A diagnosis of 'amœboma' of the colon might have explained practically all the features of this case, but the history of the case and of failure to respond to emetine injections led us to think of a neoplastic condition. The case also illustrates the fact how the true diagnosis may be missed if one depends only on



Fig. 1.—Showing hæmorrhagic eruptions.



Fig. 2.—Showing hæmorrhagic eruptions.



Fig. 1.



Fig. 2.



Fig. 3.

A CASE OF SUBCUTANEOUS EMPHYSEMA : L. H. VISSCHE
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Photograph showing the swelling of upper part of the body.

the radiological report disregarding the clinical observations. The tumour in this patient was operable and was removed successfully, but the senile heart ultimately gave way.

Acknowledgments

Our thanks are due to Major A. T. Andreasen, I.M.S., Professor of Surgery, and to Dr. B. P. Tribedi, Professor of Pathology, Medical College, Calcutta, for the operation and the histological report respectively.

A CASE OF SUBCUTANEOUS EMPHYSEMA

By LOIS H. VISSCHER, M.D.

Superintendent, Memorial Hospital, American Presbyterian Mission, Fatehgarh, U. P.

THE patient, a Hindu male aged 18 years, was admitted to the hospital on 10th April, 1945, complaining of a swelling of the upper part of his body, and of difficult breathing. The history was that he had been perfectly well and able to work, free from cough and fever, until six days previously, when he had first noticed symptoms of a 'cold' with slight cough and fever. On the same day he began to complain of mild pain on both sides of the chest; also on that day he first noticed slight swelling of the upper part of his body. In the course of the day the chest pain rapidly increased in severity; two or three days later it subsided. The swelling of the upper part of the body progressed steadily in extent and degree. Two days before admission he began to have difficulty in breathing. On the day of admission, during the ox-cart ride to the hospital, his face became so swollen that his right eye was closed (see photograph, plate XXIV). His dyspnoea also became severe.

Past history was not obtainable; the patient was too dyspnoic and his companions were not members of his immediate household.

Physical examination revealed a well-developed, well-nourished young man, acutely ill, with laboured respirations. He was crouching in a frog-like position, trunk bent forward. He spoke in a hoarse voice, with great difficulty. He coughed frequently, raising a thin, frothy, greenish sputum. His face and neck were very swollen, as in severe nephrosis. His arms and upper trunk were also swollen, but the legs and the lower trunk were normal in appearance. Palpation revealed much subcutaneous crepitation in all the swollen areas. Temperature 101.6°F. (oral). Pulse 120. Respiration 28. Blood pressure 120/80. Chest: respirations rapid; expansion appeared equal; no supraclavicular retraction and no use of accessory muscles of respiration; chest resonant throughout, with suggestion of 'crack-pot' resonance on the left side. Vesicular breath sounds were heard throughout, but fainter on the left side. The

crepitation of the subcutaneous air beneath the stethoscope prevented auscultation. Heart: apex beat palpable in the sixth interspace, two inches within the nipple line. Right border behind sternum. Rate rapid. Tonus strong. Impossible to auscultate. The rest of the physical examination was negative.

Laboratory report: urine showed one plus albumin, one plus pus cells; otherwise negative. Blood: 70 per cent Hb (Sahli); R.B.C. 2,600,000; W.B.C. 9,000; differential: polymorphonuclears 74 per cent, lymphocytes 15 per cent, large monocytes 11 per cent. Sputum: no acid-fast bacilli found in the one specimen examined.

X-ray of the chest showed many subcutaneous tissue planes outlined by gas; partial left pneumothorax with 20 per cent collapse; diffuse mottling throughout both lung fields, interpreted as advanced bilateral tuberculosis.

A hypodermic needle was put into the distended subcutaneous tissues of the neck, and about 50 c.cm. of air was aspirated with difficulty. The air was not under pressure, and did not seem to be collected in any large pockets. Left thoracentesis was done (with artificial pneumothorax apparatus), and the intrapleural pressure was found to be negative during inspiration, and positive during expiration. After about 1,000 c.cm. of air was withdrawn with difficulty the interpleural pressure became negative during both inspiration and expiration. However, these aspirations did not at all relieve the patient's dyspnoea or discomfort.

The patient remained critically ill with rapid pulse and respiration. He was very apprehensive. He insisted on crouching on his knees, with his trunk bent forward. He was given 25 c.cm. 25 per cent glucose intravenously every eight hours; also 1 per cent ephedrine nose-drops every four hours, in the hope that he might inhale a little. (No spray apparatus available, and no oxygen available.) He received chloral and bromide mixture every four hours, but did not sleep, or get relief from his apprehensiveness. His condition remained unchanged for the first 24 hours; then the pulse rate rose to 130 and the respiratory rate to 34. Again small amounts of air were aspirated from the neck tissues without any relief of symptoms. Since he had had no sleep for at least 48 hours, the patient, 36 hours after admission, was given morphine sulphate grains 1/6. He immediately fell asleep; the respiratory rate dropped to 20; the pulse decreased to 80, and became weak. Caffeine sodium benzoate was injected. Forty-five minutes after receiving the morphine, the pulse rate was 64 and the respiratory rate 12. Fifteen minutes later the patient expired.

Obviously he should not have received the morphine. The question remains, what form of therapy might have offered some chance of saving his life. Tracheotomy was frequently considered, but rejected because there was no supraclavicular retraction, or other evidence of

laryngeal obstruction. The references to subcutaneous emphysema which I have seen all state that it is rarely serious; yet the patient was in a dying condition even before receiving the morphine.

A CASE OF CEREBRAL MALARIA WITH UNUSUAL ONSET

By SURJYA KUMAR BHOWMICK, L.M.F.

Telepara Tea Estate, Binnaguri P. O., Jalpaiguri Dist.

ON 19th July, 1946, at 2-45 p.m., a coolie girl aged 5 years old was admitted into the Telepara Tea Estate Hospital in a semi-conscious state with frequent vomiting.

History.—The patient, while playing at about 12 noon in front of her house on the same date, was reported to have had sudden vomiting and after several vomits she fainted.

Examination.—Temperature on admission 99.2°F., pulse—140, respiration—40 per minute and regular. Lungs clear; heart nothing abnormal found; liver not enlarged; spleen 2 fingers below the costal margin; no rigidity of neck; limbs flaccid; pupils contracted; reflexes present and equal on both sides; knee-jerk slightly present; Babinski's sign absent.

Examination of blood showed a heavy infection with *Plasmodium falciparum* rings.

She was at once given an injection of quinine hydrochloride grs. 5 with coramine 1 c.c. intramuscularly. Soap water enema was given. As the patient passed urine in bed during my examination no catheterization was done. Hot foot bath and cold application over head by a continuous flow of water were continued.

At 6-45 p.m., the temperature went up to 102.2°F., respiration was 50 per minute, pulse could not be counted and the patient became completely unconscious. An injection of quinine hydrochloride grs. 1½ with coramine ½ c.c. in 10 c.c. of glucose solution was given intravenously. Coramine 1 c.c. every 30 minutes after was continued intramuscularly.

In spite of all the measures the patient died at 10-30 p.m.

A CASE OF VINCENT'S ANGINA TREATED WITH PENICILLIN, SOLUSEPTASINE AND THIAZAMIDE

By S. C. GANGULI, L.M.F.

A. M. O., Dhelakhat T. E., Tinsukia

A HINDU male, aged about 34 years, was admitted in the hospital on 14th April, 1946, for the treatment of anæmia and scabies, and was progressing satisfactorily.

At 11 a.m. of 21st April, 1946, he suddenly developed high fever, became delirious and the inside of the throat and the neck was swollen.

Dyspnoea and hoarseness of voice appeared gradually. Throat swabs were taken and fusiform bacilli were found on microscopic examination.

Soluseptasine 10 c.c.m. (5 per cent solution) was injected intramuscularly at once but all the above complaints increased rapidly and at 4 p.m. the axillary temperature was 105°F.

At 4 p.m., penicillin 20,000 units was given intramuscularly and the same dose was given after 3 hours and after that 10,000 units intramuscularly was given at 3-hourly intervals up to 10.30 p.m. of 23rd April, 1946. In total 210,000 units of penicillin were given. Soluseptasine 10 c.c. intramuscularly thrice daily was also continued up to 23rd April, and then the patient was given orally thiazamide 2 tablets (1 gramme), thrice daily up to 27th. Besides these dettol gargle, antiphlogistine to the neck and glucose intravenously were given.

The patient began to improve from 11 p.m. of 21st April. Next day the axillary temperature was 101°F. to 102°F. Temperature came down to normal on 23rd noon, and other symptoms disappeared except hoarseness of voice which remained for 3 more days. The patient was quite well on 27th April.

The cause which I could elicit was a dirty tea brush stick used in cleaning the mouth.

I had a similar case in my practice about 7 years back and in that case soluseptasine 10 c.c.m. (5 per cent solution) intramuscularly at 4-hourly intervals was given but the patient died within 24 hours.

My thanks are due to E. D. Hooper, Esq., Acting Manager of the Tea Estate, for allowing me to report this case.

Therapeutic Notes

NOTES ON SOME REMEDIES

II. PALUDRINE*

By R. N. CHAUDHURI, M.B., M.R.C.P. (Edin.),
T.D.D. (Wales)

Professor of Tropical Medicine, School of Tropical Medicine, Calcutta

Introduction

IN the chemotherapy of malaria there are two major problems, one concerning the radical cure of vivax infection and the other its prevention in persons who are exposed to the bite of infected mosquitoes—properties which neither quinine nor mepacrine possesses. Until recently

* This article does not represent the observations that are now being made in India on this drug. Much of the information given has been gathered from Curd, Davey and Rose (1945) and Davey (1946).

not much progress was made, and this may have been due, in part at least, to a wrong conception of the pathogenesis. We have accepted as an established fact Schaudinn's observation that the sporozoites which transmit malarial infection from the mosquito to the vertebrate host penetrate red blood cells directly, and grow and multiply there, although there is a period of days or weeks following the mosquito bite when no parasites can be demonstrated in the blood; we did not bother about the immediate fate of the sporozoites, and we were satisfied as long as we could quickly rid the blood of the parasites. But it is now known that, at least in bird malaria, the parasite undergoes a period of development in the tissues of the vertebrate—hence called 'exo-erythrocytic (e e) stage'—before the red blood cells are invaded, when of course the clinical symptoms appear. Although not yet satisfactorily demonstrated, there is circumstantial evidence that a similar cycle occurs, as first suggested by James and Tate, in all species of malarial parasites, so there are at least three stages in their life cycle, viz, the sporozoites, the tissue phase and the blood phase. These e e forms serve as a reservoir for the release of blood forms, but they appear to be transient in certain infections such as *Plasmodium falciparum* and persistent in others such as *P. vivax*. They are very refractory to quinine and mepacrine, and are the root causes of relapses. It thus follows that this hitherto hidden aspect of plasmodium which links the sporozoites and the later forms in the blood is of paramount importance in any consideration of chemotherapy, a point stressed by S. P. James for some years, and offers most reasonable explanation of the present problems in the treatment of malaria. While more light is needed to clear up still obscure points the above hypothesis has formed the basis for recent researches on antimalarial drugs. The aim has been to find a true causal prophylactic drug that would act against either the sporozoites or the e e forms and thus prevent parasites from ever appearing in the blood, and preferably it should be equally active against the blood forms. Judging from the results already achieved we seem to be more on the right track now.

New researches

The work carried out by Curd, Davey and Rose in the Imperial Chemical Industries in Manchester in the search for a better antimalarial drug began by a study of various forms of avian malaria, and at the same time chemical work on the synthesis of speculative drugs was started. For various reasons they decided to explore fields away from the quinolines to which belong quinine and pamaquine, and the acridines which include mepacrine, and eventually they came to find noteworthy activity in certain pyrimidine substances. The first of them, 2666, prepared in 1942, proved to be inactive against human malaria in safe doses,

but modifications of its chemical composition led to the discovery of 3349 in the next year, and it gave therapeutic results comparable to those obtained with mepacrine or quinine. The subsequent development of the work took them to biguanidine substances, and so far two of them, viz, 4430 and 4888, have exhibited quite outstanding antimalarial properties. Both were found to destroy not only the asexual forms circulating in the peripheral blood, but also the e e forms. The latter drug, however, has a more pronounced action and seems to be the best drug at the present moment. Paludrine, as 4888 has been named, was first synthesized in November 1944 and submitted to the Liverpool School of Tropical Medicine early next year for clinical trials under the supervision of Adams, Davey and Macgrath. The field tests have been carried out by Hamilton Fairley and his colleagues at the Australian Army Research Unit at Cairns in Queensland.

Pharmacology

Two salts of paludrine are in use at present, the hydrochloride for oral treatment and the acetate for injection. The hydrochloride is an odourless, white crystalline powder with a bitter taste. It is slowly soluble in water and an aqueous solution of it can be boiled without affecting its stability. The acetate is similar to the hydrochloride but is more soluble in water. After oral administration, the drug is absorbed rapidly and reaches maximum concentration in the blood within two or three hours. If it is given twice daily, say in 500 mg. dosage, there is a build-up of plasma concentration which rises rapidly to its maximum in two or three days, but it falls rapidly after the cessation of the drug owing to its excretion which occurs chiefly through the kidneys. Even after heavy and prolonged dosing, the concentration falls below the present limit of estimation (i.e. 30 microgrammes per litre) within a week, and the drug cannot be detected in the urine a few days later. This fall both in plasma and urinary level is considerably faster than has been observed with mepacrine. The general distribution of the drug in the body is similar to that of mepacrine, but the concentrations in the white cells and in organs such as the liver are much smaller, while the concentrations in the erythrocytes are about four times as much as in the plasma.

Action in human malaria

The work at Cairns fully confirms the earlier studies made in England and indicates the value of paludrine as a causal prophylactic, as a clinical suppressive, and as a therapeutic agent in vivax and falciparum malaria. In small doses it has a complete and permanent effect in preventing falciparum parasites gaining access to the blood stream, i.e. it has a sterilizing action on the presumed e e forms. It is therefore a true causal prophylactic. A person living

in a malarious country should get complete protection against this type of malaria with a daily dose of 25 mg. or with 100 mg. (one tablet) twice weekly, and if it be continued for two or three weeks after the last exposure to infective bites, it would sterilize the infection. In the case of vivax malaria, paludrine has an inhibitory and not lethal effect on the e e forms, but the parasites do not appear in the circulatory blood as long as a daily dose of 100 mg. is being taken. In either form of malaria mepacrine has no such action, i.e. it does not prevent parasites coming into the blood, which suggests that the two drugs have different modes of action and tends to confirm the presence of e e forms in human malaria. However, with paludrine, in the case of vivax infection, sometime after the cessation of the drug overt attacks of malaria occur, but the intervals between the attacks are significantly longer than with mepacrine. It therefore appears that paludrine is not a true causal prophylactic against this form of malaria, but a daily dose of 100 mg. is sufficient to suppress it completely.

In the treatment of clinical cases, the efficacy of paludrine has also been confirmed. A dose of 100 mg., thrice daily for ten days, has produced complete cure in falciparum malaria. There is rapid clearing of asexual parasites from the peripheral blood accompanied by effective control of the temperature and clinical recovery of the patient. In vivax malaria, however, no radical cure can be guaranteed. The same treatment is given as in falciparum malaria, but it is better to follow it with one tablet once a week for six months to prevent relapses (*vide infra*). Another method that has been suggested is a combination of paludrine (100 mg.) and pamaquin (10 mg.) given three times a day for ten days, the reason being that pamaquin is supposed to act on the e e forms and lower the relapse rate, and that by combining the two drugs the relapse rate will be still further lowered.

Some noteworthy results have been obtained with single doses of paludrine, and are likely to lead to important developments in practice. Thus one dose of 50 to 100 mg. has been found to afford complete protection against falciparum malaria when given soon after exposure to infected mosquitoes. A single dose (*viz*, 300 mg.) also achieves a *clinical* cure in both vivax and falciparum malaria, but experiments are in progress to find out the best single dose treatment. It is highly probable that in B.T. infection a weekly instead of daily dose of 100 mg. (as mentioned earlier) will prove to be an effective suppressive in which case a satisfactory method of preventing relapses would be to give a single dose of paludrine once a week for an indefinite period after therapeutic control of the primary attack. The advantages of a drug that need to be taken once a week as a prophylactic are obvious, and so also are the advantages of single dose clinical cures in a

country where the vast majority of patients do not care to undergo radical cure or to take measures against fresh infection.

Like quinine or mepacrine paludrine has no action on the sporozoites nor does it prevent the appearance of gametocytes of either *P. vivax* or *P. falciparum*. However, it has been shown that so long as the patients are receiving the drug, and for a week after the last dose, the gametocytes are not infective for mosquitoes, they fail to develop while in the stomach of the mosquito owing to the action of the drug. Finally, quartan malaria responds to it with doses as low as 50 mg. given twice daily, but not enough cases have been treated to warrant general conclusions; similarly, there has not been enough experience with parenteral administration, but doses of 100 mg. have been given without producing any toxic manifestations, and on the other hand doses as low as 5 mg. seem to have a marked effect on the course of the disease.

Toxic action

This is insignificant when a total of less than 1.0 gramme is given in twenty-four hours in two or more doses. Minor toxic symptoms may be encountered when 1.0 gramme per day is given. These include vomiting, epigastric pain and evidence of irritation of the renal tract such as presence of red cells and a few hyalin and granular casts in the urine. Marked, but not necessarily dangerous, toxic signs may be expected from the administration of single doses of 1.0 gramme, and these may assume the form of diarrhoea or hæmaturia.

Conclusion

Thus it is seen that paludrine is not only very effective in dealing with active malaria, but that it also has a remarkable action in protecting against the bite of infected mosquitoes. Even a single dose, *viz*, 3 tablets—100 mg. each, controls a clinical attack, and relapses are prevented if it is followed by one tablet once a week. It represents an important advance on mepacrine and quinine. It is free from the unpleasant skin-staining associated with mepacrine and appears to be safe since no toxic effects have yet followed its use in dosage far beyond what is therapeutically effective. As it is chemically less complex than mepacrine, it should be easier to produce and may therefore be cheaper. Its full potentialities have yet to be explored and extensive clinical trials are still proceeding.

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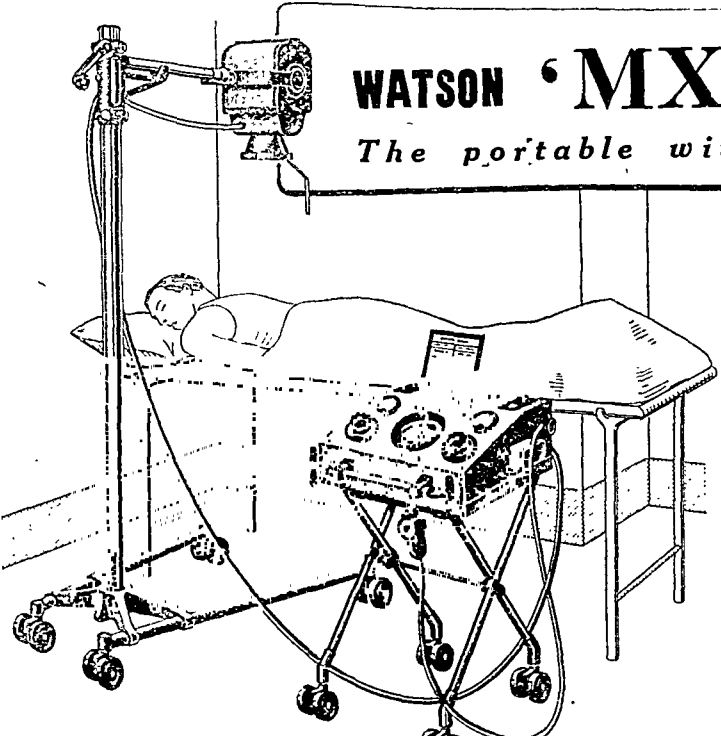
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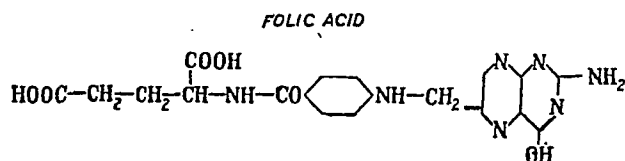
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Indian Medical Gazette

OCTOBER

SYNTHETIC FOLIC ACID

THE following formula of this effective drug has been published :—



N-[4-(2-amino-4-hydroxy-6-pteridyl) methyl amino benzoyl] glutamic acid.

It is a yellow powder.

There are, it is stated, two methods of preparing the compound. One of them utilizes common laboratory reagents and should not present much difficulty (*Lancet*, 1946b).

The drug cures : (1) Pernicious anæmia by oral administration of 20 to 40 mg. daily. The maintenance dose is small, 5 to 15 mg. daily : it may be even smaller. No intolerance or allergic effects have been noted (Kaufmann and Schwager, 1946). (2) Nutritional macrocytic anæmia. In this type of anæmia there is no achlorhydria and no need for a maintenance dose of a liver preparation : otherwise it is like pernicious anæmia. Conclusive reports have been published (*Lancet*, 1946a). A recent Indian study is being reported in this issue (page 402) by Das Gupta and Chatterjea. (3) Macrocytic anæmias of infancy. These anæmias of obscure genesis react very well (*J.A.M.A.*, 1946). (4) Sprue. Doses of 15 mg. intramuscularly, daily, for 3 weeks have benefited remarkably, if not cured, undoubted cases of sprue (Derby, Jones and Johnson, 1946). (5) Chronic diarrhoea. A series of 6 Indian cases has been reported. The patients also suffered from an iron deficiency type of anæmia. The diarrhoea was checked but the anæmia remained (Carruthers, 1946). (6) Agranulocytosis in experimental animals. The condition was present in rats due to deficiency of folic acid in diet and action of succinyl sulphathiazole (*Lancet*, 1946a).

Being non-toxic and easy to administer, folic acid is likely to be tried in all blood dyscrasias, nutritional disorders and chronic morbid states of the alimentary tract. In the near future it is bound to supersede liver extracts which need patients of pernicious anæmia for their assay and plentiful supplies of liver of good quality for their manufacture. At present it is available in small quantities, for clinical trials, under proper conditions.

Lately doubts were entertained as to whether an easy process of synthesis of folic acid had been found or even the synthesis been effected (*Lancet*, 1946a).

Folic acid was originally derived from liver, yeast and green leaves, including green grass, was thought to be another constituent of the vitamin B complex and named Bc. It was also known as Folvite (Kaufmann and Schwager, *loc. cit.*). Folic is an adjective from *foleum*, a leaf. With such a derivation its therapeutic action in anæmias and diarrhoeas is not unexpected.

Another preparation from green leaves, which shall be nameless, is also a good therapeutic agent for many complaints, although because of its entirely proprietary nature it has not been much commented upon in the medical press. All flesh is grass.

Incidentally, should the pronunciation be fō'lic (ō as in go) or fol'ic (o as in or)? We prefer fō'lic in view of *foleum*. Another example is bō'ric in view of Bōron (unfortunately, it is also pronounced bor'ic).

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Medical News

HEALTH CONDITIONS IN INDIA DURING 1945 SLIGHT INCREASE IN BIRTH RATE

THAT on the whole the birth rate in India in 1945 seems to have increased over the rate in 1944 but it did not reach the level of the last intercensal years, is shown by the Preliminary Note on Health Conditions in British India during the year 1945 by the Public Health Commissioner with the Government of India.

Nativity.—In previous years there had been a progressive decline in the birth rate in British India. From a birth rate varying round the figure of 34 per one thousand during the last intercensal years it came to 29 per one thousand in 1941 and to 26 in 1943 and 1944. This reduction in the recorded birth rate was shown by nearly every province, the only difference being that in some the reduction was more pronounced than in others. Whether this decreasing birth rate was 'due to a real decline in fertility rates; to a changed age-sex composition or is merely a transient phase—the result of passing conditions' cannot be stated with certainty; for an elaborate analysis would be necessary before any authoritative pronouncement could be made on the subject, states the Note.

The available figures for 1945 indicate an increase in birth rate compared to the corresponding figures in 1944 in U. P., Bihar, Orissa, Bengal, Assam, C. P., Delhi and Ajmer-Merwara. A small lowering of birth rate is reported in the case of N. W. F. P., Sind, Madras and Bombay. In the case of Coorg and the Punjab not much deviation from the rate in 1944 is shown.

Mortality.—The monthly total mortality figures received from the provinces show that the general health situation in the year under review was far from favourable in certain provinces. In Bihar, Orissa, Bengal, the Central Provinces and Bombay mortality was above the medium level of the 1937-41 quinquennium. The situation in C. P. was particularly bad. While 'in the absence of any special investigation', the Note says, 'it would be difficult to say how far this unfavourable situation was due to wartime strains on the health of the public', it seemed 'not unlikely that in many cases the food situation, overcrowding and the difficulties that all administrations experienced in maintaining properly staffed and equipped health services were factors that contributed not a little to the general worsening of health conditions'. In the remaining provinces the position was fairly satisfactory. Mortality in the Punjab was below the normal.

Epidemics and other diseases.—There were violent outbreaks of epidemics in several parts of the country. Cholera raged high in U. P., Bihar, Orissa, C. P., and Bombay. Smallpox occurred in a virulent form in U. P., Bihar, Orissa, Bengal, C. P., and Madras. The country was comparatively free from plague except Bombay where it broke out in an epidemic form in certain parts of the province.

Mortality recorded under fevers in 1945 in Bihar, Orissa, Bengal and C. P., and Ajmer-Merwara was above the median level in the quinquennium 1937-41. Mortality recorded under the miscellaneous group 'all other causes', which excludes the diseases already mentioned and respiratory diseases, dysentery and diarrhoea, was abnormally high in C. P. and Delhi throughout the year.

THE INDIAN JOURNAL OF RADIOLOGY

At the first Indian Congress of Radiology, held at Madras during 13/16th February, 1946, it was decided to publish a journal entitled 'The Indian Journal of Radiology' under the auspices of the above Association. This will be published quarterly and will be supplied to all members of the Association and also to Radiologists all over the world.

The editors, Dr. P. Rama Rau and Dr. K. M. Rai, solicit original articles or case reports for publication in the journal. The journal will be published on art paper, and radiographs, illustrations, skiagrams, etc., if any, will be reproduced.

INDIAN PORTS AGAINST WHICH QUARANTINE RESTRICTIONS WERE IN FORCE ON 9TH SEPTEMBER, 1946

Against port or place	Imposed by	Date	Disease
Calcutta (Air)	..	9-9-36	Cholera.
Calcutta "	..	19-2-38	Smallpox.
Bombay "	..	9-9-40	"
Allahabad "	..	5-8-46	"
Delhi "	..	5-8-46	"
Calcutta "	..	16-8-45	Cholera.

Against port or place	Imposed by	Date	Disease
Bombay (Air)	Transjordan	24-2-46	Smallpox.
Calcutta (Sea and Air)	"	1-3-46	"
Madras "	Ceylon	22-3-45	"
Bombay "	"	19-1-46	"
India "	Iraq	16-12-45	"
India "	Persia	21-3-45	Cholera.
India "	"	21-8-45	Smallpox.
India "	Egypt	11-4-45	"
India "	"	8-8-46	Cholera.
India "	China	18-8-46	Smallpox.
India "	"	18-8-46	Enteric fever.
India "	"	18-8-46	Cholera.
India "	Burma	6-12-45	Smallpox.
India "	Bangkok	12-3-46	Cholera.
India "	"	12-3-46	Smallpox.
Calcutta "	Malayan Union.	21-6-46	Cholera.
Cawnpore (Air)	"	10-9-46	"
Bombay (Sea and Air)	"	21-6-46	Smallpox.
Calcutta "	"	21-6-46	"
Delhi (Air)	"	21-6-46	"
Chittagong (Sea)	"	21-6-46	"
Madras (Sea and Air)	"	10-7-46	"
Calcutta "	Singapore Colony.	21-6-46	Cholera.
Cawnpore (Air)	"	10-9-46	"
Bombay (Sea and Air)	"	21-6-46	Smallpox.
Calcutta "	"	21-6-46	"
Delhi (Air)	"	21-6-46	"
Chittagong (Sea)	"	21-6-46	"
Madras (Sea and Air)	"	3-7-46	"
India "	Sarawak	10-7-46	Cholera.
India "	"	10-7-46	Smallpox.
Calcutta "	Labnan (British Borneo).	10-7-46	Cholera.
Bombay "	"	10-7-46	Smallpox.
Madras "	"	10-7-46	"
India "	Philippine Islands.	7-7-46	"
India "	"	7-7-46	Cholera.
India "	Sourabaya	13-8-46	Smallpox.
Calcutta "	"	"	Cholera
Calcutta "	"	"	Typhoid.
Calcutta "	"	"	Paratyphoid.
Calcutta "	"	"	Smallpox.
Calcutta "	Netherlands Indies.	26-6-46	"
Bombay "	"	26-6-46	"
Madras "	"	8-7-46	"
Chittagong (Sea)	"	26-6-46	"
Delhi (Air)	"	26-6-46	"
Calcutta (Sea and Air)	Hong Kong	23-7-46	Cholera.

THE BOON OF INSULIN

By L. E. SESSEL

(From Release No. F. 79 of United Kingdom Publicity Services, New Delhi)

TWENTY-FIVE years ago, two Canadian doctors in their twenties proved that a substance called Insulin could be extracted from the pancreas of animals, and that injections of this substance controlled diabetes in dogs. Dogs were chosen as being, biologically, the most suitable agents for the doctors' experiments, but the young scientists' goal was to benefit mankind.

As a result of their investigations it has come about to-day that hundreds of thousands of diabetic men and women of all nations, all ages and every class of society have obtained relief from the use of the beneficent drug. Their lives have been indefinitely

prolonged, and a miraculous change in their outlook has been wrought.

Much scientific and other progress had to be made by Frederick (later Sir Frederick) Grant Banting and Charles H. Best, a twenty-two-year-old medical student, between the time when they had satisfied themselves of the effective use of Insulin on dogs and the moment when mankind could derive full advantage from its powers. The extract from the pancreas—now available from oxen, sheep and pigs, and coming chiefly from South America—had to be obtained in large quantities, had to be purified for human tests, produced on a large commercial basis and at a much lower cost, and standardized for treatment. The work on production itself was undertaken, by scientific workers other than Banting and Best.

By the earliest processes only 15 units of Insulin were available from each ox pancreas—even less unless it was processed within a very short space of time. Scientific work carried out in Britain, Denmark and the United States effected a complete transformation of conditions.

The amount of Insulin from each ox pancreas was increased from 15 units to 500 and the selling price of 100 units was reduced by stages from 25s. to 2s. 8d., thus bringing it within the reach of people of moderate means. By 1923—two years after the great discovery—production was on a large scale.

Insulin, like penicillin and vitamins, is one of the limited number of medical remedies for which an accurate dosage has been established internationally.

Improvements in effectiveness have been going on, the most important being the production of the protamine-zinc type. This has much longer action than the original discovery afforded, and an injection of it is necessary only once a day instead of twice.

'Banting and Best not only found Insulin', a writer in a recent issue of the *British Diabetic Journal* points out, 'but gave it free to the world without personal gain. What incredible millionaires they could have been had they imposed a penny royalty on a hundred units'.

But whatever financial profit they forewent, they won the more satisfying rewards of the world's gratitude, along with great fame. To Banting belongs the credit of extracting the anti-diabetic principle from the pancreas; others before him had had the idea but had failed over the process of extraction. He became Professor of Medical Research at the University of Toronto and in 1923 was awarded the Nobel Prize for Medicine, jointly with Professor J. J. R. Macleod, under whose encouragement and help the two young scientists had been working. He was tragically killed in February 1941 in an air disaster while on his way to England. He shared the Nobel Award with Best, now Director of the Department of Physiology and the Banting and Best Department of Medical Research at the University of Toronto.

Best was a member of the Canadian delegation that attended the recent Royal Society Empire Scientific Conference held in London. One of the Conference's recommendations was that—'in view of the steady increase in the demand for Insulin, the British Commonwealth should make every effort to collect, process and preserve all available pancreas'. The recommendation recorded that purified Insulin, which can be stored for long periods without loss of potency, would be needed on an increasing scale for the treatment of diabetes.

At the recent silver jubilee celebration of the triumphant discovery of the use of Insulin Best was the recipient of a silver souvenir. The celebration at the Royal Institution in London was organized by the British Diabetic Association, of which the famous author H. G. Wells was president. This organization is active in its work for the benefit of diabetics, of whom there are some 200,000 in the United Kingdom. The establishment of a Banting Convalescent Home in Britain is projected.

PATHOLOGICAL AND MEDICAL RESEARCH IN AUSTRALIA

By CHARLES LYNCH

(Reprinted from Release No. P/380 offered by the Public Relations Officer, Australian High Commissioner's Office, New Delhi)

LARGE-SCALE production of influenza virus vaccine is one of the most important activities of the Walter and Eliza Hall Institute of Melbourne, an Institute which is world-famous for its up-to-date research in pathology and medicine.

In response to wartime requests from the British and Australian Army authorities, the Institute established a pilot plant for the production of about one thousand doses of vaccine per day.

The work was done in collaboration with the Commonwealth Serum Laboratories, and when the method was worked out in detail, key personnel were trained and the process was transferred to the Serum Laboratories.

Many difficulties had to be overcome to evolve methods by which thousands of eggs half-way through incubation could be inoculated with virus, incubated for two more days and then 'harvested'.

The 'harvest' of the egg consists of the fluid which fills one of the cavities of the embryo. This fluid in the treated egg contains very large amounts of influenza virus, and after concentration and sterilization, it becomes the vaccine.

Great care has to be taken by the investigators to see that no unwanted germs are allowed to enter the egg during the process.

This research is only a phase of a wide range of activities which have made this Institute a subject of perennial interest to medical research workers in all parts of the world.

The Institute was founded in 1916, largely on the initiative of the late Sir Harry Allen, then Professor of Pathology at the Melbourne University. With various members of the medical staff, Sir Harry Allen urged that clinical research should be carried out in the modern diagnostic laboratories at the Melbourne Hospital. As a result, the trustees of the late Walter and Eliza Hall agreed to complete the pathological block of the hospital to provide accommodation for an institute of research in pathology and medicine.

The trustees arranged to make annual payments of Rs. 26,770 towards its upkeep, and this sum was later increased to Rs. 53,540 annually. In addition, the activities of the Institute have led to an expanding range of other financial support from public and private sources.

Prominent in its development was Melbourne-born Dr. C. H. Kellaway, a Director, who performed valuable work in expanding its laboratories, and who was also instrumental in securing financial support from the public. When the Royal Melbourne Hospital was moved from the heart of the city to Parkville, accommodation was found for the Institute in the modern hospital buildings.

Research Director is Australian-born Dr. F. M. Burnet, who succeeded Dr. Kellaway in 1944, upon the latter's appointment to the post of Scientific Director of the Wellcome Foundation.

Dr. Burnet, F.R.S. and Ph.D., London, was educated at Geelong College, Melbourne University and the Lister Institute, London. He specializes in virus diseases and in epidemiological work. His publications include *Biological Aspect of Infectious Disease*, and numerous technical papers.

Range of research

Many and diverse subjects have occupied the attention of the Institute's staff of skilled investigators.

Study of snakebite not only clarified understanding of the mechanism by which the venoms act, but led to production of antivenene for use in treatment. In

addition other animal poisons such as spider venom, bee venom, the venom of the platypus, and mussel poison have been investigated.

An infectious disease known as Q fever, because of its Queensland origin, was the subject of successful investigation in Australia, which can claim priority in its recognition and elucidation. Much of the credit belongs to workers in Brisbane, but the organism responsible was isolated in the Walter and Eliza Hall Institute.

Extensive studies have been carried out on immunity—the manner in which the body achieves protection against injury, whether this is caused by bacteria, by viruses, by bacterial poisons (such as those produced in gas gangrene or in carbuncles) or by animal poisons.

Other important researches have been concerned with virus diseases of man and animals such as infantile paralysis, herpes and roup with bacterial diseases, dysentery, tuberculosis; with staphylococcal toxin, with blood pigments and with the chemical detection of poisons such as lead and arsenic.

Iodine for influenza

In common with overseas countries who are devoting much attention to possible methods of killing germs like the influenza virus, the Institute has also been experimenting with antiseptic mists and vaporizers. The great activity of iodine as a killer of influenza virus has been studied by members of the virus and biochemical departments in collaboration. It has been discovered that the vapour of iodine is the most potent means of killing influenza germs.

For various technical reasons it is very doubtful whether any general use of this property could be made, but in emergency situations iodine might be extremely valuable for preventing the spread of infection when people are crowded indoors for short periods.

In the biochemical department, special attention is being given at present to the study of the chemistry of blood pigments, and the mechanism by which sugar is broken down to smaller molecules by yeast and other living cells.

A method developed by the Institute is now being used as a standard Australian method for the estimation of carbon monoxide in air, or in the blood of persons exposed to the gas. This particular work has been important to the Royal Australian Air Force, and a technician from this service was attached to the laboratory during the war to carry out the large number of analyses required.

An unexpected discovery made in the course of research was that an unimportant virus disease of mice was closely related to smallpox and vaccinia (cow-pox). The vaccine lymph, used to protect human beings against smallpox, is just as effective in protecting mice against this highly fatal smallpox. This particular research is of interest because of its immediate relationship to the very first piece of virus investigation, Jenner's discovery of vaccination with cow-pox.

At present researches are being made into the cause of tick typhus, a disease which resembles scrub typhus in many ways, but is due to a distinct type of germ. There is strong circumstantial evidence that the disease is caused by tick bite, but the full scientific proof is still being sought.

With the end of the war a department of clinical research has been created in the Institute. It is staffed wholly by men and women from the Services under the leadership of Dr. Ian J. Wood. Thanks to a generous gift of Rs. 2,14,170 from the four Melbourne racing clubs, a special ward will be erected by the Royal Melbourne Hospital for the use of the department. This will allow active research into the problems of gastric and liver disease, and should prove an important influence in maintaining a high standard of medical practice and teaching in the hospital.

Establishments such as the Walter and Eliza Hall Institute are typical of the modern and progressive outlook which is characteristic of the Australian approach to the solution of problems affecting the general health and the well-being of the community.

AN AUSTRALIAN BEATS SCRUB TYPHUS

By CECIL SLOCOMBE

(Reprinted from Release No. MNL/108 offered by the Public Relations Officer, Australian High Commissioner's Office, New Delhi)

THOUGH so small that it cannot readily be detected without the aid of a microscope, the mite carries a virus which during 1943 threatened to immobilize numbers of Australians fighting the Japanese in New Guinea.

Now, through the wartime researches of a young Australian entomologist, Robert Nicholson McCulloch, this microscopic enemy has been mastered, and a bar to peacetime development of mite-infested territory has been removed.

The mortality rate from scrub typhus is six to eight per cent high when it is considered that in certain areas a person unprotected from mites faces considerable risk of infection. Apart from the mortality danger, the scrub typhus menace had to be tackled during the war because men who contracted the disease were put out of action for at least three, and usually four, months at a time.

As is usual in advances in medical science, some men had to be human guinea-pigs. When McCulloch called for volunteers, hundreds of Australians stepped forward. From 120 in the first batch of volunteers at a North Queensland (Australia) base, 20 were selected. All had had scrub typhus before. They were subjected to infection risk, but none caught typhus.

Successful fluid

McCulloch was at that time a captain attached to No. 3 Mobile Entomological Section, Australian Army Medical Corps. He switched site of his experiments to Dobodura (New Guinea), where large numbers of troops again volunteered to aid the research work.

In McCulloch's experiments, the test subjects wore treated or untreated clothing as decided by the drawing of lots; refrained from using dimethyl phthalate (then on issue as a mosquito repellent); and proceeded with normal duties which consisted mainly of clearing grass and scrub from the camp area. Later tests included deliberate exposure to infection—the men sitting or lying for two hours a day in selected patches where mites were thick.

McCulloch made important discoveries from these tests, which proved that DDT with which clothing was impregnated became ineffective after the clothing had been washed two, three or four times. When dimethyl phthalate was used, extremely limited biting occurred after the clothing had been washed two or three times. However, troops wearing clothing impregnated with dibutyl phthalate were found to remain immune to mites after their garments had been washed as many as eight times.

DDT and dimethyl phthalate were discarded from the experiments, and dibutyl phthalate, because of its newly-discovered resistance to washing, was further investigated. Dibutyl phthalate then became standard anti-mite fluid.

Adopted by SEAC

When stocks of this fluid became adequate, there was a striking drop in the incidence of typhus. In New Guinea and the Solomons, it fell from 360 cases a month per 100,000 troops in 1943 to less than 10 a month, a year later.

Following McCulloch's researches, South-East Asia Command adopted dibutyl phthalate as a mite repellent, and recommended the Australian routine for its application to clothing. In Burma, as in New Guinea, army authorities found that presence of the mites in the jungle, and the strong chance of contracting typhus, were having a bad psychological effect on the men, so great as to represent an undermining of morale. However, for a cost of only about a shilling a man a month, the medical service was able to provide every man complete immunity.

Civilian uses

Civilians in North Queensland have widely adopted the anti-mite fluid since the war. Scrub typhus is not uncommon there, about 30 cases being the yearly average before preventive measures were found. This State is Australia's sugar producer, and during the clearing of the Mossman sugarcane area about 1,000 cases of scrub typhus occurred over a period of six years.

The Australian army method was to rub on the repellent thoroughly by hand to distribute one fluid ounce all over the shirt, trousers and socks. The fluid could be carried around in a tobacco tin, and in half an hour each man could treat all the clothes he possessed.

'While the hand treatment was considered best for the army, probably shaker bottles will be the most suitable for civilian use', says Mr. McCulloch. 'Using such bottles, a set of clothing could be sprinkled with anti-mite repellent in two or three minutes'.

An important advantage of the repellent is that it does not harm or stain clothing.

McCulloch was a 1926 Australian Rhodes Scholar. He was employed for some years by the New South Wales Department of Agriculture, but is now entomologist attached to the School of Tropical Medicine, University of Sydney. This quiet, unostentatious young Australian can be classed among the notables of field research men during recent years.

CALCUTTA SCHOOL OF TROPICAL MEDICINE. ELEVENTH CLINICAL MEETING HELD ON 7TH AUGUST, 1946

Dr. L. M. Ghosh described the case of a Hindu lady aged 55 years suffering for three years from a chronic ulcer on the sacro-coccygeal region near the anus. The ulcer was about 2 inches by 2 inches in size surrounded by a band of dark pigmented margin. The edges were undermined. She had various treatments outside. The ulcer had a foul-smelling discharge at first, and with treatment it looked clean but without any sign of healing. On account of the close proximity to the anus amœbiasis cutis was thought of but the scrapings did not show any *E. histolytica*. On a careful clinical examination the whole buttock area and some parts of both lower limbs were found anæsthetic, the anæsthetic buttock area being depigmented. The diagnosis was trophic ulcer due to leprosy.

Dr. Ghosh also initiated further discussions on a case shown at the tenth meeting with a provisional diagnosis of dermatomyositis. This girl aged 10 years was suffering for eight months with erythematous raised circular bands enclosing large areas of depigmented atrophic patches on the forehead, chest, back, left thigh and both arms from shoulder to elbows. There was slow fever up to 99°F. to 100°F. The spleen was enlarged. Urine showed faint traces of albumin. The blood picture was low normal with 3,000,000 erythrocytes and 4,600 leucocytes. Blood chemistry was normal except for a slightly high creatinine excretion in urine. The skiagram of chest was normal. Blood culture, tests for kala-azar, Kahn and W.R., and Mantoux test were negative. Penicillin had no effect, but there was slight improvement with non-specific protein therapy (milk injection) and large doses of vitamins A and D. Histopathology showed degenerative changes in the muscles and a mild toxic inflammatory change in the subcutaneous fatty tissue of non-specific origin. Dr. G. Panja could not see any muscles in the histological picture which he described as of granulomatous nature with lymphocytic infiltration of the subcutaneous fatty tissue, and was of opinion that this was a case of granulomatous lesions of non-specific origin, probably a case of granuloma annulare.

Dr. P. C. Sen Gupta described the clinical features and post-mortem findings of a case of pneumococcal

meningitis complicating kala-azar. The patient, aged about 30 years, was left in an unconscious state at the kala-azar outpatient department of the School on 2nd August, 1946, and was immediately admitted to hospital. He was emaciated, anæmic and desperately ill; respiration laboured and pulse 108/32 per minute; heart sounds weak and partly masked by adventitious sounds in the lungs. There were signs of consolidation of the lower zones of both lungs and bubbling râles were audible all over. Liver was enlarged up to one inch below the costal margin and spleen was palpable. There was a marked stiffness of the neck and the head was retracted and deviated to the left. Pupils were somewhat constricted but equal in size, and reacted sluggishly to light. Kernig's sign was markedly present, the plantar response was flexor, and knee jerks were absent. Lumbar puncture showed fluid not under pressure; about 10 c.c. were removed, the fluid was watery in colour but slightly turbid and a fibrin thread formed on keeping. The white cell count was 24,000, with neutrophils 91 per cent, lymphocytes 6 per cent, monocytes 1 per cent, myelocytes 1 per cent and plasma cells 1 per cent. Sternal puncture showed *Leishmania donovani*. The cerebrospinal fluid showed 750 cells per c.m.m.; smear did not show any bacteria. Treatment with penicillin intramuscular and intrathecally, sodium sulphapyridine intramuscularly and other supportive measures did not produce any effect and the patient died at about 1 a.m. next morning. The post-mortem findings were as follows: The meninges were congested; smear from the meninges over the vertex of the brain showed Gram-positive diplococci (pneumococci). The vertex of the brain was covered with a greenish exudate extending forwards from the parietal region. Congestion and hæmorrhage was noticed over the right parietal region. Lungs and pleural cavities: Right—grey hepatization of the middle lobe, apex showed fibrosis and three-minute cavities surrounded by fibrous tissue; the pleural cavity contained one pint of serosanguineous fluid and there were bands of adhesion to the chest wall. Left—red hepatization of the lower lobe; the pleura showed bands of adhesion to the chest wall and there was 7 oz. of serosanguineous fluid in the pleural cavity. The heart showed a white patch $1\frac{1}{2} \times \frac{1}{2}$ inch over the anterior surface of the right ventricle and another $1 \times \frac{1}{2}$ inch over the posterior surface of the right ventricle. Spleen—weight 420 gm., congested; accessory spleen present. Liver—weight 1,450 gm., mottled nutmeg appearance. Intestines showed congestion and prominence of the Peyer's patches and lymphatic follicles; ten roundworms were present.

Dr. R. N. Chaudhuri showed a case of secondarily infected liver abscess in an Indian patient aged 32. Prior to admission to the hospital he was given 15 injections of emetine and was aspirated twice without effect. On admission he was very ill, toxic and running an irregular temperature with rapid pulse, night sweats and occasional rigors. The liver was enlarged and very tender. The base of the right lung was dull with diminished breath sounds and râles. Fluoroscopic examination showed the right dome of the diaphragm considerably raised and fixed. The white cell count was 16,000. Stools showed no *E. histolytica* but the patient had dysentery a year ago. An exploratory puncture showed chocolate-coloured, offensive pus; the smear contained pus cells and streptococci. In view of the high mortality associated with open operation and in consultation with Major Andreassen the patient was put on systemic penicillin therapy and was aspirated repeatedly, 50,000 units of penicillin being injected into the abscess cavity after each aspiration. During a course of six weeks he was aspirated nine times, and about six pints of pus were withdrawn. The improvement has been striking clinically and radiologically. It is of interest to note that penicillin may replace surgical operation in secondarily infected liver abscess and lower the high mortality.

Dr. A. Wahed described a case of myasthenia gravis and one of achalasia cardia.

Public Health Section

POISONOUS EFFECTS OF D.D.T. ON HUMANS

By U. CHIT THOUNG, M.Sc. (Lond.), D.I.C.,
A.R.C.S., F.C.S.

Chemical Examiner to the Government of Burma

RECENTLY the writer received a case of food poisoning from the District Health Officer, Bhamo. In this respect two samples of rice were sent to him for examination.

According to the District Health Officer rice from which the two samples were taken was supplied by the District Supply Officer to a Frontier Force Constabulary at 'Wawang' near Bhamo sometime ago. On 29th July, 1946, the personnel of the unit mentioned above suffered from vomiting and purging about one hour after their evening meal. Some white particles were found mixed with the bags of rice used that day. Doctors and nurses rushed to the camp where they found twenty-seven men who had vomited several times; the men also complained of giddiness.

On the following morning the District Health Officer went to the camp and found altogether seventy-two men suffering from food poisoning. The typical symptoms were slow pulse, 40 to 50 per minute, giddiness when getting up and dilated pupils.

Of the two samples of rice one was found to contain about 16 per cent of D.D.T. whereas the other samples were free from it.

SOME CLINICAL IMPRESSIONS OF A PLAGUE EPIDEMIC

By D. SHAMANNA, B.A., M.B., B.S.

Assistant Surgeon, Saklaspur

and

K. V. HEDGE, L.M.P.

AN outbreak of plague occurred in the town of Saklaspur, Hassan District (Mysore State), in March 1946. The first case was an imported one, not immediately recognized as plague. While suspicion was lurking in our minds that it might be plague, cases of ratfall occurred in the town and splenic smears of such rats were positive for *B. pestis*. This finding and occurrence of other cases of human plague established beyond doubt the onset of the epidemic which continued till the end of June 1946.

All the 26 cases that came under our observation were of the bubonic type. The majority of these cases did not represent the associated signs and symptoms of plague depicted in textbooks like injected conjunctivæ, mental prostration, gastro-intestinal disturbances, etc.

Fever and adenitis were the only two signs in these cases. Perhaps we would have missed diagnosing these cases had we not been in the midst of an epidemic.

It was difficult in the early stages of the epidemic to convince the semi-educated lay patients and their semi-educated relatives that these were plague cases as these men, by their past experience, carried pictures of very severe plague infections in their minds. The cessation of fever on the 3rd or 4th day of sulphathiazole treatment in some cases was a further proof from the lay man's point of view that these were not genuine plague cases. 'Could fever come down on the 3rd or 4th day of plague? Could the buboes of plague subside without suppuration in 10 or 12 days?'—were some of the questions asked of us. In 4 cases, to these doubting Thomases we actually demonstrated the presence of *B. pestis* in the gland punctures of their patients.

We noticed a distinct difference between this epidemic and the previous ones we had handled in different places during different years, prior to the introduction of sulphathiazole, judged either from the course of the disease or the mortality rate. In the previous epidemics the mortality rate was high, while in the present one it was low. As a matter of fact the plague subjects in this epidemic were themselves optimistic of their survival.

The present epidemic itself might have been a mild one. The public health measures instituted, such as inoculations, cyano gassing, etc., might have been prompt and efficient. Still the fact became inescapable that the success we achieved in handling this epidemic was in a large measure due to the prompt and adequate use of sulphathiazole. We had read reports of the use of the drug in plague, but had an opportunity of handling it ourselves for the first time in this epidemic.

All the patients were treated in their own homes. The routine treatment adopted was that recommended by Mathur *et al.* (*Ind. Med. Gaz.*, August 1945). 'The initial dose of sulphathiazole was 2 grammes followed by a maintenance dose of 1 gramme every 4 hours, making a total of 7 grammes in the first 24 hours, on the 2nd and 3rd days the dose was reduced to 4 grammes, 1 gramme every 6 hours. This was further reduced to 3 grammes from the 4th to 6th day, making a total of 24 grammes as the standard dose. Children of 8 to 14 were given half the above dose. For combating toxæmia soluseptasine 10 per cent solution and glucose 15 c.c. of a 25 per cent solution were administered daily by parenteral route.

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every case sulphathiazole was urged continuously for 6 days, whether there were amelioration of signs and symptoms or not. Some patients ceased taking the pills from the 3rd, 4th or 5th day, as was later revealed to us.

In all 26 cases came under our treatment, out of these 7 had been inoculated and 19 uninoculated. Twenty of them had one gland (inguinal, femoral or cervical) enlarged, and 6 had an enlargement of more than one gland. The entire group included 16 males and 10 females. Children below 12 years numbered 7.

By way of complications observed during treatment, one male adult developed aphasia which lasted for 4 weeks, and two women aborted.

All the subjects were seen on the 1st or 2nd day of the onset of fever and immediately all of them were put on sulphathiazole treatment.

Eleven of these subjects took the thiazamide tablets uninterruptedly for 6 days and in them the fever came down to normal within the 5th day, and the buboes gradually subsided without suppuration within the 15th day.

In 6 of the group of 26 cases fever touched normal on the 3rd or 4th day, but reappeared about the 10th day, with increased swelling and tenderness of the glands concerned. It was made known to us that they had ceased taking the drug after the cessation of the first bout of fever. They were put on thiazamide again 1 gramme every 6 hours for another 2 or 3 days till they became afebrile. But even then, their buboes invariably suppurred and had to be incised.

Three of them touched normal temperature on the 4th day of taking the sulpha drug when they stopped taking it. But they continued to be apyrexial till about the 15th day when the buboes suppurred and had to be incised.

Six patients died in spite of the prompt exhibition of sulphathiazole; at any rate we were assured by their relatives that they had been given the drug in proper doses. Of these 5 had not been inoculated. All the six died within the 7th day of the onset of the disease. Amongst the dead 2 were children and 4 adults. The mortality rate among the treated was 23 per cent.

Amongst the survivals, 19 had not been inoculated. Eleven of those that survived, exhibited permanent subsidence of fever within the 5th day, and subsidence of buboes within the 15th day of the institution of treatment. The other 8 cases went on to suppuration of buboes but eventually recovered.

A few of the town folk stricken with plague, sought the aid of Hakims and Vaidys, by-passing us. Our advice to them went in vain. Out of sheer humanitarian motives, we even passed a hint to these Hakims and Vaidys about the virtues of sulphathiazole and indicated its dosage. To our surprise only one used the drug and that in tiny dosage of one tablet *t.d.s.* for an adult. Needless to mention, the mortality rate in this group of cases was considerably higher. To induce even the poorest of patients to have the benefit of sulphathiazole, the municipal authorities made a distribution of these tablets free of cost to all the patients that needed them. The fact that the Hakims and Vaidys did not take advantage of this, but treated their cases on their own indigenous lines, with results none too encouraging, in the face of the good results achieved and preached by us, is rather depressing.

Though the value of sulphathiazole in the treatment of plague has already been well recognized, this communication strengthens its claims as an almost domestic remedy.

Current Topics

The Absorption, Excretion and Toxicity of Streptomycin in Man

(From the *Medical Press and Circular*, Vol. 215, 17th April, 1946, p. 250)

In January 1944, a new antibacterial substance, streptomycin, was isolated from culture filtrates of actinomycosis griseus. *In vitro* this substance has a marked antibacterial action against many gram-negative and positive bacteria. Sufficient success has attended the treatment of experimental infections in animals with various gram-negative bacteria and with mycobacterium tuberculosis to warrant an extended clinical investigation of the value of streptomycin in established infections in man.

The authors now report certain preliminary studies carried out on the absorption and excretion of streptomycin in man. Brief mention is made of three cases in whom the drug was used therapeutically. Finally the toxic reactions observed are described.

The authors drew the following conclusions from the study.

Streptomycin is not absorbed after oral administration in amounts sufficient to produce detectable concentrations of the drug in the serum.

The failure of the drug to be absorbed from the gastro-intestinal tract is not due to inactivation of streptomycin by the gastric juice.

Following the intramuscular or intravenous administration of a single dose of streptomycin, 46 to 87 per cent of the dose injected can be recovered in the urine within twenty-four hours. Streptomycin is excreted more slowly by the kidneys than is penicillin. It appears likely that effective blood levels of streptomycin can be maintained by administering the drug at intervals of six to eight hours.

In patients with meningitis, streptomycin diffuses to a slight extent from the blood into the cerebrospinal fluid. The intrathecal administration of streptomycin in doses up to 20,000 units does not produce signs of meningeal irritation. With doses of 10,000 to 20,000 units an appreciable concentration of the drug can be maintained in the cerebrospinal fluid for at least twenty-four hours.

No serious toxic reactions apparently follow the injection of single doses of streptomycin in amounts up to 60,000 units or after the continued administration of the drug for periods of two to three weeks in doses totalling 2,725,000 to 18,150,000 units.

The intravenous and subcutaneous injection of concentrated solutions of the present preparations of streptomycin causes too much discomfort to warrant the use of these methods of administration.

The drug can be administered in an intravenous infusion without the production of unpleasant symptoms.

Intramuscular injections are fairly well tolerated for periods up to one or two weeks. Therapy continued beyond these times may cause severe discomfort.

Three cases of infection due to gram-negative bacillus and treated with streptomycin are reported; no conclusions concerning the efficacy of streptomycin can be drawn from them.

From other sources the abstractor has heard more favourable reports about streptomycin. It appears to be complementary to penicillin. It has a place in the treatment of chronic carriers of dysentery bacilli; it is reported to be a valuable treatment for influenza meningitis and to have had beneficial results in the treatment of acute miliary tuberculosis. So far no test samples have been received in this country from U.S.A.

Myasthenia Gravis and the Thymus

(From the *Lancet*, i, 18th May, 1946, p. 746)

THE operation of removing the thymus to relieve the symptoms of myasthenia gravis was introduced in the United States in 1941. The first extensive series was reported a year later in this country by Keynes and Carson; of 12 patients submitted to operation, 3 died and 7 were completely, or almost completely, relieved of symptoms. The hope expressed at that time—that this surgical experiment was the beginning of a real advance—has now been largely fulfilled, as is evident from the report, on another page, of a recent meeting of the Royal Society of Medicine. In the series described the decline of mortality associated with operation may be attributed to further experience in managing the stormy post-operative period and to the skill of Keynes, though he modestly described himself as a carpenter carrying out the physicians' directions. Dr. Purdon Martin made it clear that the operation can be received with only qualified approval. But it is equally evident that until the biochemical changes in myasthenia gravis can be controlled by other methods it will continue to help sufferers otherwise doomed to a miserable lingering existence and a probable early death.

The Insomnia of Heart Failure

(From the *Lancet*, i, 18th May, 1946, p. 747)

THE therapeutic value of a good night's sleep is nowhere more evident than in patients with heart failure; yet these people are often peculiarly resistant to soporific drugs. Wheeler and White suggest a possible reason for this. In their view insomnia may be the presenting symptom of left ventricular failure, and in patients with hypertension, aortic stenosis, aortic incompetence, and extensive myocardial infarction the cause of the insomnia may be pulmonary congestion, even though no basal crepitations are present. Inquiry usually reveals that these patients have dyspnoea on exertion and that though they do not complain of nocturnal dyspnoea, they are more comfortable sitting up than lying down. Even in cases where the diagnosis of left ventricular failure is obvious, it is not always realized that the sleeplessness is due to this orthopnoea, and vain attempts are made to control it with hypnotics. Ultimately sleep may improve because of the onset of right ventricular failure which temporarily

relieves the pulmonary congestion, but by this time the patient is likely to be beyond the reach of any form of treatment. On the other hand, if the cause of the insomnia is appreciated in the early stages there is a good prospect of bringing relief to the failing myocardium by rest and the administration of digitalis, or, if the condition has progressed too far to respond to these measures, by a course of organic mercurial diuretics with a low-salt diet. Moreover, by reducing the pulmonary congestion, this treatment will relieve the insomnia.

The World's Food

(From the *Lancet*, i, 18th May, 1946, p. 745)

THE April issue of the *Nutrition Bulletin* analyses the world food situation. It says that Russia has expanded her grain production in the areas that were not occupied, but the last harvest in the liberated areas amounted at best to 80 per cent of the pre-war average. There has been a serious shortage of tractors and draught animals, as well as fertilizers of animal origin. Russia is transferring 1½ to 2 million tons of grain to Poland, the Danubian countries, and France. Britain, which is not a food-exporting country, has surrendered only a few thousand tons of potatoes; the 900,000 tons of food sent to the continent in 1945 was stock from overseas that was built up here for the purpose of relief.

The two main factors that have produced the world food shortage are war destruction and drought, but the position has been further complicated by floods in China, New Zealand, and Queensland. Apart from these unpredictable adversities, however, we have failed to estimate the probable yields and the probable demand for grain. Estimates of stocks had to be drastically revised downwards at the end of last year; the error seems to have been due partly to miscalculation of the amount of wheat likely to be fed to livestock in the North American countries, and partly to weakness in the statistical methods. No serious measures were taken to replenish the reserves of grain, which were rapidly diminishing throughout 1945. In Britain the policy of ploughing up the land was reversed, more grain was fed to stock, and the extraction of flour was lowered from 85 per cent to 80 per cent. In the great wheat-producing countries the acreage under wheat was about 16 per cent below what it had been in 1938. Governments and farmers in these countries hastened to reduce their large reserves, which they considered might be unmarketable after the end of hostilities; much was either fed to stock or converted into commercial alcohol for the manufacture of rubber; and in the Argentine a large amount was used for fuel. We are paying to-day for the restrictionist farming policy which was accepted by all the main producing countries before the war. The only possible solution would have been the establishment, after the Hot Springs conference of 1943, of a supreme inter-allied council to decide the programme of food production. As it was, the Combined Food Board in Washington continued to represent only Britain, Canada, and the U.S.A. At no time did UNRRA have any decisive voice in cropping and production programmes or in allocation. The new International Food and Agriculture Organization was not in existence at the end of the war, and control passed virtually into the hands of Canada and the U.S.A.; since September last, probably three-quarters or more of the exportable surplus of wheat has lain in the North American continent.

The U.S.A. is endeavouring to conserve grain, and to apply to relief all that is available. The next three months will be among the most difficult in the world's history; after that everything will depend on the harvest. An attempt to pass on the blame from one country to another would be fatal. We must accept the warning that the food economy of the world is now so far integrated that it must be studied as a single problem in production and distribution.

Deaths After Carbarsone

(From the *Lancet*, i, 27th April, 1946, p. 631; 'correspondence')

SIR,—Two deaths have lately come to my notice as a result of the use of carbarsone in normal quantities given for amoebiasis. One of these cases was as follows:

A woman of 32, previously healthy, was treated for amoebiasis with 1 gramme of chiniofon daily by mouth for 8 days. Her condition improved. Two weeks later abdominal pain returned, together with diarrhoea. The patient was given carbarsone (Lilly) in the usual quantity of 0.25 g. twice daily. On the 8th day of this treatment, fever and headache resulted, and the carbarsone was discontinued after she had received 3.75 g. Next day general symptoms of meningitis were observed. She was admitted to the Municipal Hospital 'Hadassah' in Tel-Aviv and died there 5 days later. Necropsy showed a hæmorrhagic encephalomyelitis.

I should like to know whether there have been any records of similar deaths after the administration of this drug in the usual dosage. This is of particular importance to us because amoebiasis is a common disease in our institutions.

CENTRAL OFFICE OF THE SICK
FUND, TEL-AVIV, PALESTINE.

JOSEPH MAYER,
Medical Director.

[A woman of 55 years, who received 5 g. of carbarsone by mouth in 10 days for diarrhoea of unknown cause, died after developing acute fatty degeneration of the liver and exfoliative dermatitis. Ervin Epstein, who recorded this case in 1936 (*J. Amer. Med. Assoc.*, 106, 269), could not find any record of other fatalities from carbarsone in therapeutic doses.—Ed., L.]

Streptomycin

(From the *British Medical Journal*, i, 30th March, 1946, p. 492)

WE referred recently (Feb. 23, p. 278) to the use of streptomycin for the chemotherapy of tuberculosis. There are numerous other infections—notably those due to various Gram-negative bacilli—which may prove amenable to this substance, and the growing volume of American literature dealing with it is a measure of the hopes entertained for its future. Of all the innumerable antibiotics studied during the past few years streptomycin appears to be the only one combining a wider range of antibacterial activity than that of penicillin with such freedom from toxicity that parenteral injections of large doses are harmless. Discovered two years ago by Waksman and his colleagues, it is extracted from cultures of *Actinomyces griseus*, and has been obtained and used clinically in varying degrees of purity. Weight for weight it appears to be less active than penicillin, and the unit of activity is also even smaller: it is defined as that quantity which when dissolved in 1 ml. of broth will just prevent the growth of a standard strain of *Bact. coli*. A unit of penicillin so defined, with *Staph. aureus* as the test organism, would be roughly one-fiftieth of what it is, and the existing unit has been condemned as inconveniently small; why that of streptomycin has been so fixed that an ordinary daily dose runs well into seven figures is not clear.

Several groups of workers have studied streptomycin pharmacologically. When given by the mouth it is scarcely absorbed at all, but retains activity and appears in high concentration in the faeces. For systemic effect it can be given subcutaneously, intramuscularly, or intravenously; it is then excreted by the kidneys, but more slowly than penicillin, with the result that injections at intervals of six hours suffice to maintain a therapeutic blood level. Like penicillin it must be given intrathecally in order to produce a therapeutic level in the cerebrospinal fluid, but it passes from the blood into other body fluids. No serious

toxic effects have been seen, but injections into tissues may be painful and into veins may cause thrombosis; fever, urticaria, and headache have also been observed. To what extent impurities are responsible for such effects is not clear.

Streptomycin has naturally been exploited chiefly in infections due to bacteria insusceptible to penicillin. One of the earliest reports—that of Reimann *et al.*—described the treatment of 5 cases of typhoid fever: these occurred in a single epidemic with unusual features, including an exceptionally prolonged course; treatment was started in some of the cases at a late stage, and the strain of *Bact. typhosum* was less susceptible *in vitro* to streptomycin than most. Even allowing for these unfavourable features, the results were not decidedly encouraging. The same may be said of the two cases of septicæmia due to Gram-negative bacilli described by Anderson and Jewell. On the other hand they appear to have cured a patient with *H. influenzae* meningitis. Three cases of this condition, all treated with good results, are included in the series of 45 cases of various infections treated with streptomycin at the Mayo Clinic, and described by W. E. Herrell and D. R. Nichols. These infections include coliform septicæmias, chiefly associated with severe urinary tract infection, and simple urinary infections, in most of which results were good; several cases of undulant fever, in only one of which a really striking effect was obtained; and 5 cases of bronchiectasis treated by inhalation as well as intramuscular injection with 4 successes. *Bact. friedländeri* was eliminated from the sputum of 2 of these patients, and ozæna due to this organism seems also to have responded to some extent. The treatment of syphilis in 4 patients was followed by relapse. While the efficacy of streptomycin in some of these and other conditions mentioned cannot yet be assessed, there seems to be no doubt of its striking all-round efficacy as a urinary antiseptic. H. F. Helmholtz has shown that *in vitro* all five species of bacteria commonly found in urinary tract infections are suppressed by a concentration only one-fifth of that attained in the urine by ordinary systemic dosage. No other drug has so all-embracing an action.

Streptomycin is still not generally available in U.S.A. It is being supplied there to one or two hospitals, and is also being used for the treatment of men in the Forces injured in the war. When manufacture is well under way in the States we may expect supplies over here.

One-Shot Treatment of Acute Gonorrhœa with Penicillin: Review of 617 Male Cases

By T. R. LLOYD JONES, M.R.C.S.

E. M. DONALDSON, M.B. (Edin.), D.P.H.

and

S. J. ALLEN, M.D. (Belf.)

(Abstracted from the *Lancet*, i, 13th April, 1946, p. 526)

A NEW vehicle for prolonging the action of penicillin, consisting of magnesium sulphate monohydrate in peanut oil, was described. Magnesium sulphate was selected as being readily obtainable, non-toxic in the dosage to be used and possessing in high degree the hygroscopic properties desired. Monohydrate was preferred to magnesium sulphate exsiccatus B.P. because of its known chemical purity. 2.25 gm. of monohydrate per 10 c.cm. of the ol. arachis was taken as the preparation remains fluid at room temperature and could be injected without difficulty through a 19 B.S.W.G. needle. In preparing the magnesium sulphate suspension it is essential that all materials and utensils should be sterile and free from moisture. The formula consists of 2.25 gm. of magnesium sulphate monohydrate mixed with 300,000 units of sodium penicillin and suspended in 10 c.cm. of ol. arachis so that 1 c.cm. of suspension contains approximately 250,000 units of penicillin. The preparation can be

stored at room temperature without any significant loss of potency up to 2 months.

Penicillin had been demonstrated, as determined by the capillary tube technique of Fleming using *Staphylococcus aureus* (Oxford) as the test organism, in the sera of 8 out of 11 patients, 24 hours after a single subcutaneous injection of 250,000 units in this vehicle contained in 1 c.cm. of the suspension. Subcutaneous injection gave better clinical results than did the same dose injected intramuscularly. After injection patients were returned to full duty. Excepting local reactions in 50 per cent cases there was no toxic effect.

Short-term results as judged by 1 week surveillance in 617 cases of gonorrhoea treated by various single-injection methods are given: 87 per cent were cured with one injection. Of the 80 cases of failure 71 showed a prompt response by a second injection and 9 by the third injection, 5 of these last group had foci of infection in prostate, vesicles or urethra for which local treatment was given. In a subsequent series treated by this preparation and method this treatment has cured 108 out of 113 patients pursuing their normal activities in contrast to the hospital patients reported by Romansky.

A. B. R. C.

Methylene Blue Test for Bilirubin

By J. SEIDE, Ph.D., M.D.

(Abstracted from *Acta Medica Orientalia, Jerusalem*, Vol. 5, No. 4, April 1946, p. 123)

The technique of the test is as follows:—A drop of 0.2 per cent aqueous solution of Loeffler's methylene blue is added to 5 c.cm. of urine. If the test is positive the solution turns into a brilliant green colour immediately. A crude estimate of the amount of bilirubin present in the urine may be made by further adding the methylene blue solution drop by drop till the blue colour appears again. From the number of drops of methylene blue required to change the colour to blue again a rough quantitative estimate of the bilirubin present may be made assuming that two drops of the methylene blue solution corresponded roughly to 0.1 mg. of bilirubin. In case of negative result the mixture remains dark blue.

The author claims that the test is sensitive and gives positive results in all cases where the liver is involved, for example, in hepatic diseases chronic or acute whether accompanied by jaundice or not, in infective epidemic hepatitis, in cardiac enlargement of the liver, hepatic cirrhosis and carcinoma. A slightly positive reaction is not uncommon in pernicious anaemia, malaria, cholecystitis and lead intoxication. Fallacies occur when yellow or brown dyes given in medicine appear in the urine or when blood is present.

The test appears to be useful in evaluating the course of the disease. An increase in the number of drops needed for reverting the colour of the urine from green to blue would indicate that the liver damage is progressing—a decrease would suggest improvement. The test allows an early diagnosis at a time when jaundice of the skin or sclerae is not yet visible.

The test cannot be stated as a new invention as it was described by Torday and Klier as early as 1909. It was then left in a hibernating state till Franke revived it in 1931.

The test cannot be however considered to be specific for bilirubin.

J. P. B.

A Note on the Use of Penicillin in the Laboratory Diagnosis of Whooping-Cough

By P. M. ANDERSON

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 23rd February, 1946, p. 244)

A METHOD for incorporating penicillin into culture media for the isolation of *Hæmophilus pertussis* is

described. *Hæmophilus pertussis* was isolated from 79 to 154 patients by means of the penicillin plate method, and from only 39 of them when ordinary medium was used.

Enteric Fever due to *Bacterium enteritidis* var. *blegdam* (*Salmonella blegdam*) : A Series of Fifty Cases in Australian Soldiers from New Guinea

By F. FENNER

and

A. V. JACKSON

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 9th March, 1946, p. 313)

1. Fifty cases of *Bacterium enteritidis* infection in Australian soldiers are described. The organism was further identified as *Bacterium enteritidis* var. *blegdam* in 17 cases. The remainder conformed to the clinical and epidemiological picture of the confirmed cases and during convalescence the majority of specimens of serum examined gave specific agglutination reactions with a formolized emulsion of *Bacterium enteritidis* var. *blegdam*.

2. The disease is probably endemic throughout New Guinea, New Britain and the Solomon Islands, and cases have occurred among natives and Japanese in these areas.

3. Clinically, cases fall into two main groups: firstly, enteric fever (salmonella fever) of a fortnight's duration, and secondly, an illness which commences in the same way but in which complications develop owing to localization of infection from the second week onwards.

4. Complications include cystitis, epididymo-orchitis, periostitis, perichondritis, cholecystitis, broncho-pneumonia, empyema, pericarditis and arteritis.

5. Malaria occurred coincidentally in a high percentage of cases among Australian soldiers.

6. *Bacterium enteritidis* var. *blegdam* can be isolated from the blood in the first and second weeks of the disease, and from the faeces and urine in a large number of cases from the second week onwards. In cases in which infection is localized, it can be isolated from the appropriate abnormal fluids.

7. A slight neutrophile leucopenia is present in the first and second weeks of the disease.

8. No specific treatment is known.

The Present Status of Oral and Nasal Cold Vaccines

By L. E. GLYNN

and

H. E. GLYNN

(Abstracted from the *Pharmaceutical Journal*, Vol. 156, 13th April, 1946, p. 241)

In a status report on the use of vaccines for the common cold authorized for publication by the American Council on Pharmacy and Chemistry and the Council on Industrial Health, 1944, it is concluded that 'decisive evidence of the value of any vaccine is not forthcoming, and the weight of careful studies clearly indicates that none of the vaccines now available when administered by the routes advised have proved of value. . . . At present any attempt to prevent colds by the use of vaccines must be recognized as purely experimental. . . . and any proposal to administer such a vaccine, if given at all, should take this into consideration. As in all measures of a purely experimental nature, the uncontrolled use of any cold vaccine now available should be discouraged'. Wilson and Miles go still further and consider it 'most unfortunate that countenance should be given to the use of a

vaccine so clearly devoid of protective power, and all those concerned with public health should set their faces resolutely against a practice which, though financially profitable for the makers of the vaccine, is without any scientific support'.

Primary Atypical Pneumonia

By A. B. ADAMS *et al.*

(Abstracted from the *British Medical Journal*, i, 16th February, 1946, p. 227)

CLINICAL and laboratory findings in a series of 50 cases of primary atypical pneumonia are reported.

Among the findings were: (a) Increasingly positive cephalin-cholesterol flocculation reactions during the course of the disease in the majority of cases. (b) The presence of a positive heterophil antibody reaction (horse cells) to a titre of 1 : 448 or higher in 36 per cent and to a titre of 1 : 224 or higher in 62 per cent of the cases.

Profitable avenues for further research seem to be indicated by these findings.

The importance of the lateral film in diagnosis and accurate location is stressed.

An Allergic Reaction following Typhus-Fever Vaccine and Yellow-Fever Vaccine due to Egg Yolk Sensitivity

By S. S. RUBIN

(Abstracted from the *Journal of Allergy*, Vol. 17, January 1946, p. 21)

WITH the increased use of virus and rickettsial vaccines prepared from infected chick embryo and chick egg yolk sac, we can expect to see various allergic manifestations due to egg and chicken sensitivity.

Swartz reported a systemic allergic reaction induced by yellow-fever vaccine in an allergic individual who was sensitive to egg white and chicken meat. Sulzberger and Asher reported three cases of urticaria and erythema multiforme-like eruptions appearing thirty-six or more hours after yellow-fever vaccine inoculations. Accompanying the skin manifestations were general malaise, joint pains, headache, fever, pruritus, nausea, and vomiting. According to Sulzberger, the clinical picture, the incubation period, and the course of the manifestations suggest a sensitization or an allergic mechanism identical with mild serum sickness, rather than an infectious or direct virus effect.

This report is that of a soldier who developed angio-neurotic oedema, blocking of the nose, and tightness in the chest shortly after receiving typhus-fever and yellow-fever vaccines. The interesting finding in this case is that an allergic individual gives a history of egg yolk sensitivity which was definitely corroborated by various tests.

Nevertheless, it is not the purpose of this paper to decry the efficacious use of these important prophylactic agents. Instead, we merely wish to report that allergic manifestations do exist in egg and chicken-sensitive patients and that, once this fact has been established, it necessitates the cautious administration of the vaccine, by giving it in small increasing doses and by having epinephrine and a tourniquet on hand.

The Oral Manifestations of Iron Deficiency

By W. J. DARBY

(Abstracted from the *Journal of the American Medical Association*, Vol. 130, 30th March, 1946, p. 830)

THE representative cases studied are interpreted as indicating that iron deficiency alone may be manifested by fissures at the labial commissures and a superficial glossitis. Such an interpretation is consistent with the experience of Suzman, who reported four cases of

Plummer-Vinson's syndrome with such oral lesions which healed rapidly following iron administration.

Furthermore, Waldenström reported four cases of such oral lesion accompanying hypochromic anaemia which responded to treatment with iron alone. He implied that an additional four patients in his series showed similar responses. All of these experiences confirm the conclusion of Waldenström that these lesions of the mucosa and the dysphagia are both cured by sufficient administration of iron with no other therapy.

That these lesions are often confused with the oral signs of B complex deficiencies is evident from the therapeutic measures which were first instituted in most of the cases reported. The records of these individuals cover a sufficient period of time so that there is no doubt of the ineffectiveness of B vitamin preparations and of the efficacy of iron. No relapses during iron therapy have been observed in any of these subjects, in contrast to some of the reported cases of ariboflavinosis. The therapeutic response to iron has been rapid (one to three weeks), again in contrast to the lesions of the tongue attributed to 'chronic niacin deficiency'. The regeneration of the lingual papillae in iron deficiency has not been influenced by the administration of B complex vitamins.

It is of interest to point out that a number of the cases of glossitis or perleche which have been reported as yielding slowly to vitamin therapy or of relapsing during or immediately following treatment have been accompanied by anaemias of the degrees seen in the cases here reported. Further, on occasions the use of combined iron and vitamin therapy has led to the disappearance of oral lesions, and the success has usually been attributed to the vitamins.

It is not my intention to deny that a deficiency of riboflavin, niacin or other B complex factors may and sometimes does give rise to glossitis or cheilosis. Rather, it is emphasized that another cause of these signs is iron deficiency.

The Pathogenicity of Penicillin-Insensitive Infection

By H. R. S. HARLEY *et al.*

(Abstracted from the *British Medical Journal*, i, 27th April, 1946, p. 639)

IT is the object of this paper to show that, in the East at any rate, infection of wounds with penicillin-insensitive organisms is common and must be taken seriously; and it is hoped that further interest will be stimulated in this important subject. Our observations are confined to infection with the three Gram-negative organisms—*Bact. coli*, *Ps. pyocyanea*, and the *Proteus* group—on the one hand, and penicillin-insensitive strains of *Staph. aureus* on the other.

They are the cause of a major proportion both of fulminating and of prolonged low-grade infection in bone following war wounds.

When using penicillin tubes for the local instillation of penicillin into wounds every possible precaution was frequently ineffective in preventing the appearance of Gram-negative infection. Such infection occurred in 50 per cent of our cases, and was often responsible for the breaking down of wounds. Breakdown was liable to occur even in soft-tissue wounds when the secondary invader was a penicillinase-producing strain of *Bact. coli*. Pus associated with the presence of *Ps. pyocyanea* or *Proteus* group, on the other hand, could usually escape or be expressed from the depths of a soft-tissue wound, which then healed in a satisfactory manner. In the case of soft-tissue wounds infected with penicillin-insensitive organisms there was no instance of severe toxæmia following suture under local penicillin. In this respect our observations coincided with those of workers in Europe, but when closure of femoral fractures was undertaken it soon became apparent that Gram-negative infection was anything but innocuous.

Since in the compound femoral fracture it is notoriously difficult to perform a complete primary wound

excision, it is not surprising that it is this type of injury that both penicillin-sensitive and penicillin-insensitive organisms persist after the primary operation. It was amongst the compound femoral fractures that most of the complications associated with Gram-negative infection were encountered. When attempts were made to carry out delayed primary suture on or about the fifth day after wounding it was appreciated that infection, uncontrolled by both penicillin and the sulphonamides, was being locked up in the wound.

This led to the abandonment of delayed primary suture for compound fractures of the femur. The safer procedure of secondary suture with drainage after bacteriological examination was adopted instead. An initial wound swab was taken when the case arrived between three and five days after wounding, but no attempt at suture was made. Local procedures were limited to the removal of foreign bodies, correction of displacement, and, if necessary, more free exposure of the fracture site to ensure adequate drainage. The fracture was appropriately immobilized after the application of an occlusive dressing. Systemic penicillin was combined with the giving or completion of a 40-g. course of sulphathiazole. Although there were exceptions under this treatment, to be referred to later, it was the rule to find that the patient became apyrexial within ten days, and that both local and general conditions remained, or became, satisfactory. It was found that many of the wounds became free of pathogens and that secondary suture performed at this stage was followed by a smooth post-operative course. At the time of secondary suture the fractured bone ends were no longer visible in the depths of the wound, and closure of the latter was more on a par with closure of a soft-tissue injury. Even if the initial wound swab yields a penicillin-insensitive organism, free drainage combined with sulphathiazole should limit the spread of infection at this stage. Secondary suture with drainage performed on the tenth or twelfth day, when tissue planes are already sealed off and local adjustments have occurred, should give rise to no anxiety provided the bone is not involved.

Penicillin-insensitive strains of *Staph. aureus* were found at the forward-base level in wounds affecting any part of the body, but it was in the compound femoral fracture that they proved most troublesome. Many of the wounds appeared clean, and suture was performed on or about the fourth day after wounding. Some cases gave most gratifying results, but many others developed complications ranging from wound breakdown to spreading sepsis and secondary hæmorrhage, and in many cases this was due to the presence of a penicillin-resistant *Staph. aureus*. It was soon realized that it was unwise to carry out closure of a compound femoral fracture without first excluding the presence of a penicillin-insensitive staphylococcus. In the East delayed primary suture without bacteriological control is a dangerous procedure in the case of compound fractures of the femur; it is much safer to perform secondary suture on the tenth or twelfth day after a knowledge of the infecting microbes has been acquired.

It has been our clinical experience that where surgery is adequate a dosage of 20,000 units of penicillin every three hours, given by the intramuscular route, will control a staphylococcus whose sensitivity is equal to that of the Oxford staphylococcus, but that it will not control a more resistant organism. The more insensitive strains can be controlled provided that the dosage is stepped up sufficiently.

Sudden Death following Initial Injection of a Mercurial Diuretic

By A. MURPHY

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 27th April, 1946, p. 589)

A CONSIDERABLE literature has accumulated in regard to both immediate and delayed toxic effects of the mercurial diuretics.

Wexler and Ellis, writing in 1944, record two fatalities in sixteen months at the Boston City Hospital, during which period 5,200 ampoules of 'Mercurpurin' were used. They also state that it is only within the past two years that widespread interest has arisen concerning these accidents. All immediate fatalities have followed employment of the intravenous route, but it would appear that of those recorded, only three have resulted from the first injection.

Pines, Sanabria and Arriens, as a result of experimental work on dogs, have shown that death is due to direct toxic action of the mercurial compound on the myocardium of the ventricles leading to ventricular fibrillation, cerebral symptoms being a purely secondary effect of circulatory failure. (This is also the conclusion of other investigators.) They hold that the addition of 0.5 millilitre of a 20 per cent solution of magnesium sulphate to the mercurial diuretic prevents fatal reactions and increases the diuresis; they suggest its use whenever the intravenous route is chosen. This is a welcome discovery, as intravenous injection has several advantages over intramuscular injection; with proper technique it is painless, and free from the risk of producing tissue necrosis when a needle of inadequate length fails to enter muscle owing to gross subcutaneous oedema.

Of the four fatalities accompanying the first injection three have occurred in patients suffering from nephrosis, furthermore, nephrotics appear to provide the majority of the recorded deaths, yet they must constitute a small percentage of patients treated with mercurial diuretics. The incidence of fatal reactions therefore is much higher in this condition than in any other; but attempts to discover the reasons for this have so far proved fruitless. Irritability of cardiac muscle would be enhanced by inadequate oxygenation, and would thereby facilitate the precipitation of ventricular fibrillation by a direct cardiac poison. Search of the available literature seems to deny the existence of oedema of heart muscle itself, and further, reveals no evidence of hindrance of oxygen transfer by a low plasma protein level; yet alterations in osmotic pressure afford an attractive foundation for theory. The low pulse pressure may have been a factor in this case.

One other point deserves consideration. In view of the fact that aminophyllin is now incorporated in most mercurial diuretics ('Neptal', 'Mercurpurin', 'Salyrgan', 'Esidrone') is it possible that at times this drug can be incriminated? Merrill has reported three fatalities immediately following intravenous injection of aminophyllin; but the condition of each patient was such that sudden death might reasonably have been expected as a natural outcome of the disease process. Nevertheless, the manner of death in the subject of this report closely resembles the description of the effect on animals of a fatal dose of caffeine (another xanthine) given by Goodman and Gilman.

Since the incident recorded, 0.5 millilitre of a 20 per cent solution of magnesium sulphate has been added to all intravenous injections of mercurial diuretics given by the author to both cardiac and nephrotic subjects, with favourable effect and complete freedom from untoward reactions of any kind.

Observations on Human Leprosy : Infection of Rats with Human Excretal Organisms

By J. W. FIELDING

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 27th April, 1946, p. 578)

1. BOTH patients with advanced leprosy and others with receding clinical manifestations pass organisms in the excreta. These organisms are in large numbers, and in the latter type of case constitute a carrier problem, which points to the necessity for laboratory and hygienic control.

2. These human excreta organisms are capable of invading the skin of rats, producing by superinvasion

light internal infection. There was also in some rats evidence that partial immunity had developed.

3. Leprous blood, when hæmolyzed and inoculated subcutaneously, gives rise to early primary lesions in rats; this suggests its use for the early diagnosis of human leprosy.

4. Climate is considered to be of secondary importance to hygiene in the dissemination of leprosy. Solar radiation in dry areas is probably effective in destroying viability of faecal organisms evacuated on soil; wet areas and incidental vegetation afford some protection to such organisms.

5. Viability of the organisms appears to be destroyed by heating to 58° or 60°C. for a short time, or by extended freezing; short-period freezing tends to lower the viability.

6. If stored dry at room temperature for periods up to two years, rat excreta organisms remain viable and invasive and produce early lesions on subcutaneous inoculation.

7. The incubation periods calculated from infection to the appearance of lesions appears to depend on high viability of bacilli and on superinvasion, early neural leprosy being probably like glandular leprosy of rats—a product of early invasions of bacilli.

8. Superficial regional lesions are dependent more on superinvasion than on metastasis.

9. Both human beings and rats with leprosy pass in the excreta numerous organisms capable of invading the skin of rats and of producing intracellularly. Increased virulence is associated with intracellularity of organisms. This is suggestive of a closer affinity between the bacillus of Hansen and that of Stefansky.

The Ætiology and Treatment of Blepharitis: A Study in Military Personnel

(Abstracted from the *Military Surgeon*, Vol. 98,
April 1946, p. 279)

1. A LARGE series of blepharitis cases in military personnel were subjected to therapeutic study with the following five groups of medications: (1) Antiseptic or germicidal drugs, including silver nitrate, zinc sulphate, yellow oxide of mercury, ammoniated mercury, oxy-cyanide of mercury, bichloride of mercury, tincture of iodine, salicylic acid, sulphur, resorcin, quinolor, and merthiolate. (2) Drugs, including gentian violet and brilliant green. (3) Sulphonamide drugs, including sulphathiazole and sulphadiazine. (4) Antibiotics, including penicillin and tyrothricin. (5) Vaccines, including staphylococcus toxoid, toxoid combined with vaccine, and stock and autogenous vaccines.

2. Seborrhœic blepharitis responded best to the following treatment: (1) Daily mechanical cleansing of the lid margins, (2) frequent expression of the meibomian glands, (3) applications of $\frac{1}{4}$ per cent silver nitrate solution to the conjunctiva and 1 per cent silver nitrate to the lid margins twice weekly, (4) twice daily applications of an ointment containing 1 per cent yellow oxide of mercury and 1 per cent salicylic acid to the lid margins, and (5) treatment of associated seborrhœic dermatitis of the scalp, brows, external ears, etc. Sulphathiazole and penicillin applied in ointment form were ineffective.

3. Staphylococcic blepharitis responded well to topical treatment with the following preparations listed in order of efficacy: penicillin, sulphathiazole or sulphadiazine, and mercurials, including ammoniated mercury and a combination of 1 per cent yellow oxide of mercury and 1 per cent salicylic acid. Administration of staphylococcus toxoid proved to be an important supplementary procedure. Other measures of therapeutic value included topical application of tincture of iodine, gentian violet, and brilliant green to the lid margins. Treatment of other staphylococcic infections of the face or scalp was important.

4. In staphylococcic blepharitis a close correlation between the sensitivity of the staphylococcus strain to

penicillin and the clinical response of the disease to topical penicillin therapy was noted.

5. Staphylococcic blepharitis complicated by meibomitis was much more resistant to therapy than uncomplicated blepharitis.

6. The four cases of diplobacillary blepharitis which occurred responded completely and rapidly to topical application of sulphathiazole in ointment form.

7. Mixed seborrhœic and staphylococcic blepharitis proved to be more resistant to therapy than either form separately. It was found best to treat the seborrhœic factor first and to give particular attention to expression of the meibomian glands. After lid margin scrapings had become negative for *Pityrosporum ovale*, anti-staphylococcic treatment with sulphathiazole or penicillin ointment was employed. Staphylococcus toxoid was a valuable supplementary treatment.

8. Contact dermatitis as a result of allergy to both penicillin and sulphathiazole was observed but did not occur often enough to prejudice their use.

9. In pure seborrhœic blepharitis conjunctivitis was an infrequent complication and was readily controlled by the use of mild antiseptics; there were no corneal complications. In pure and mixed staphylococcic blepharitis conjunctivitis and keratitis were serious complications requiring conjunctival treatment with anti-staphylococcic agents. The importance of the lid margin infection as the primary focus was obvious in all cases.

10. While local chemotherapy with the sulphonamides and penicillin constitute a great advance in the treatment of staphylococcic blepharitis, the results of this series indicate that therapy is still not entirely satisfactory, especially in cases complicated by meibomitis.

Post-Mortem Findings: Prefrontal Leucotomy

(From the *British Medical Journal*, i, 11th May, 1946,
p. 728)

THE operation of prefrontal leucotomy is still in an experimental stage. It has had some brilliant though partial successes. In the catatonic schizophrenic, violence and aggression that have persisted for years have given place to quiet and relatively human behaviour; and the chronic melancholic who has proved refractory to convulsion therapy has been restored to a state of well-being by having the white fibres of his frontal lobes cut. These benefits have had to be paid for with a diminution of some of the higher faculties, and in many cases the anticipated benefit has not been achieved. One of the most serious disadvantages of the operation has been the unpredictability of the results. It has long been recognized that this is partly because the operation is a blind one, and the extent and location of the intended destruction of white matter are not controlled. Post-mortem investigation of anatomical changes and their correlation with degree of improvement have been badly needed.

A beginning in this direction has now been reported by Meyer and Beck. They have investigated 9 such cases, with a tenth in which frontal lobectomy had been carried out for basal meningioma in a mentally normal patient. In 4 of these patients—3 schizophrenics and one psychopath—clinical improvement over 8-36 months was considerable, and death eventually occurred from unrelated causes. Two patients died within a week of the operation, and the other three showed no improvement; in one of them the improvement obtained was offset by a severe frontal lobe syndrome. The extent of the surgical lesion varied very greatly from case to case, and in the patients who improved tended to be less than in the others. In one case marked improvement resulted from a unilateral operation, and in another case with a good result the prefrontal region had not been involved. Extensive hæmorrhage and a too posterior cut yielded unfavourable results. It seems that patients chronically ill and with much deterioration of personality did less well

and required a more extensive severance of the fibres than others. Considerable improvement may take place without cutting the fasciculus cinguli or other midline structure, which had been considered by Freeman and Watts to be of importance in relation to recovery.

Pathological examination has disclosed interesting anatomical findings. Retrograde degeneration of the dorsal medial nucleus of the thalamus occurred in all cases in which thalamocortical fibres had been severed. Owing to the varying extent of the operation it was possible to gain detailed knowledge of the organization of the thalamocortical radiation, which, it was learned, is in the human brain similar to that in apes. Evidence was obtained that the thalamic radiation to the orbital areas of the prefrontal region is of considerable strength. In the prefrontal cortex anterior to the cut there was a slight reduction of the number of nerve cells, particularly of the third layer. The centre median nucleus of the thalamus, which is thought to serve as a purely thalamic association centre, varies greatly from subject to subject, both in the normal and in the abnormal, and its possible significance to psychiatry calls for study.

The work of Meyer and Beck is of high interest to the neurosurgeon and the psychiatric therapist. But the chief lesson to be learned is that the operation of prefrontal leucotomy is a human experiment in which further study is urgently required.

Studies in the Control of Scrub Typhus

By R. N. McCULLOCH, B.Sc.Agr. (Sydney),
B.Sc. (Oxon.)

(Abstracted from the *Medical Journal of Australia*,
Vol. 1, No. 21, 25th May, 1946, p. 717)

THE author carried out researches in the various areas in different theatres of the far eastern war with the object of protecting troops against scrub typhus by impregnating clothing with various miticides such as dimethyl phthalate, dibutyl phthalate and a mixture of dimethyl phthalate and DDT. The investigations also included studies of the toxicity to mites of treated cloth, different methods of applying treatment to clothing and other cognate matters. Dibutyl phthalate at a dosage rate of one fluid ounce per set of clothes has been recorded as giving protection until exposure ended at twenty-two days, the clothes having been cold-water washed eight times. Dimethyl phthalate and DDT gave very much less satisfactory protection. The author claims that the treatment with dibutyl phthalate proved capable of giving practically complete freedom from scrub typhus.

D. N. R.

A Contribution to the Endocrine Aspect of the Impotence Problem : A Report of Thirty-Nine Cases

By HARRY BENGAMIN, M.D.

(Abstracted from the *Urologic and Cutaneous Review*,
March 1946, p. 139)

A SERIES of 39 impotent men with no organic or exclusively psychological causes were subjected to androgenic therapy. Treatment with testosterone propionate applied in 25 patients resulted in eight favourable sexual responses (32 per cent). The incidence of improvement was somewhat higher in the group of 14 men receiving methyl testosterone medication with seven of them reporting gratifying results (50 per cent). Thus in functional impotence increase in sexual power may be expected with androgenic treatment in one out of three or one out of two patients. Since large amounts of the hormone may suppress pituitary function temporarily and thus aggravate the

sexual inadequacy or may stimulate growth of dormant cancer cells in the prostate, doses not higher than 10 mg. testosterone propionate, twice or three times a week, seem advisable. Larger doses are indicated in selected cases only. The preferred dose of methyl testosterone is 30-40 mg.

About 70 per cent of the patients presented experienced a general feeling of well-being; however, to expect the full return of youthful vigor in elderly men would be unwarranted.

The endocrine aspect of importance constitutes but a small part of the entire problem. In the majority of cases, psychic factors play the dominant rôle. Fear and inhibitions, overwork, and excessive worry are constant destroyers of sexual competence. A thorough physical examination of every case is indispensable. Also a study from a psychological standpoint is imperative since the personality make-up and life situation of the patient must be taken into account. It is necessary to consider sexual deficiency as a symptom, not as a disease, and every case must be handled individually. Androgenic treatment can be helpful in the management of impotence even if the origin of the disorder is not entirely endocrinogenic. But hormone therapy should be supplemented with non-endocrine measures as circumstances may require.

A. B. R. C.

Penicillin Spray by Bulb Atomizer

By FRANK W. MORSE, M.D.

(Abstracted from the *Canadian Medical Association Journal*, Vol. 54, May 1946, p. 450)

PENICILLIN spray produced by hand atomizer was used by 30 patients with various respiratory infections. Observations on this series of cases suggest that the use of penicillin spray from a hand atomizer is effective in respiratory infections. The method is easy, inexpensive and just as generally applicable as sulfonamide therapy, yet has no dangers. This method warrants further trial on a large number of cases. The most striking effects of aerosol penicillin are lessening cough, sputum and toxicity.

The technique of spraying is described thus:— 'Empty lungs thoroughly by exhaling strongly and slowly. Place atomizer tip in mouth just inside teeth and on beginning inhalation, press atomizer bulb; continue rhythmic spraying throughout inhalation then stop. Hold breath at full inspiration as long as possible, then exhale slowly and gently through the nose. Continue this for 10 minutes at beginning, then for 10 minutes in an hour, then every four hours when awake. It is important to exhale strongly to empty lungs before beginning spray, but after the first inhalation, do not expire too thoroughly since some penicillin spray may be blown out of the lungs. The important point is to hold the breath as long as possible at the end of the spray inhalation, thus allowing the penicillin to be deposited in the lungs and respiratory tract. Inhalation should be slow and not too deep, otherwise coughing may be started'.

All the doses are dispensed in 4 drachms of water excepting uncomplicated sinusitis, sore throat and otitis media, when 2 drachms are used. The total dosage varies with the clinical response, but the usual period for treatment is 4 to 6 days.

Pneumonia.—(a) Severe, 24-hour dosage, 100,000 units, spray every 4 hours. (b) Moderate, 24-hour dosage, 60,000 units, spray every 4 hours. (c) Mild, 24-hour dosage, 40,000 units, spray every 4 hours.

Bronchitis.—(a) Severe, 24-hour dosage, 60,000 units, spray every 4 hours. (b) Moderate, 24-hour dosage, 40,000 units, spray every 4 hours.

Sinusitis, laryngitis, tonsillitis and otitis media.—For these conditions 2 drachms of water containing dosages similar to bronchitis is advised and inhalation is only gentle.

A. B. R. C.

Tularæmia—A Problem in Diagnosis

By EWEN A. MACKENZIE, M.D.

(Abstracted from the *Canadian Medical Association Journal*, Vol. 54, May 1946, p. 485)

A RARE case of tularæmia of so-called typhoid type was described, the other recognized types being ulceroglandular and the less common conjunctivo-glandular types comprising 85 per cent of cases and so-called glandular type comprising 15 per cent of cases. This case came with signs and symptoms of pneumonia later developing intestinal symptoms raising a suspicion of typhoid. A chance recollection of the observation 'tularæmia owing to its rarity is frequently misdiagnosed typhoid or pneumonia' gave the final clue to a correct diagnosis. No evidence of primary focus nor any palpable lymph glands was obtained. Any contact with wild rabbits was stoutly denied but as an afterthought the patient observed that she had 200 tame rabbits at home before some sickness or other had almost wiped them out. Further questioning revealed that rabbit meat had been their staple article of diet for almost two months and whereas she killed and cleaned them, her husband handled them only in the cooked state and remained well. The cat, however, was not so fortunate, a meal of raw rabbit having resulted in a brief and fatal illness. So in this case the skin or lungs seem the probable portal of entry since the husband was not affected.

A. B. R. C.

Angina Pectoris and Tobacco

(From the *Journal of the American Medical Association*, Vol. 131, 11th May, 1946, p. 142)

THE term 'tobacco angina' has been employed for many years; its importance lies in the concept that smoking tobacco may constrict the coronary arteries and thus adversely affect the heart. Recently Pickering and Sanderson studied several patients who developed cardiac pain of an anginal nature following smoking. One patient was subjected to many tests and careful studies without evidence being found that smoking produced coronary vasoconstriction; when the patient smoked before or during exercise, tolerance to exercise was not reduced. All the evidence, the authors say, was consistent with the view that smoking by this patient was a factor in producing anginal pain because it increased the work of the heart through the pulse rate and blood pressure. The use of tobacco, most cardiologists agree, is not the primary cause of coronary sclerosis, which is the pathologic lesion underlying angina pectoris. In the patient studied most completely, smoking produced anginal pain only in the period shortly after the disappearance of the pain produced by effort, and this occurred only if the pulse rate rose sufficiently. The British investigators believe that their studies provide an alternate hypothesis to the theory that constriction of the coronary arteries by tobacco is the cause of anginal pain precipitated by smoking; namely, that tobacco acts in this respect only by its effect on increasing the work of the heart. The investigation further casts doubt on the usefulness of the term 'tobacco angina'.

Gastroscopy in Acute and Chronic Hepatitis

By LIEUTENANT-COLONEL J. BANK
and

CAPTAIN C. H. DIXON

(Abstracted from the *Journal of the American Medical Association*, Vol. 131, 11th May, 1946, p. 107)

1. GASTROSCOPY of the gastric mucosa in 43 cases of acute and chronic hepatitis did not reveal significant evidence of gastritis.
2. The minimal findings observed in some patients were not considered contributory to the patient's gastrointestinal symptoms.

The Fenestration Operation for Otosclerosis

By G. E. SHAMBAUGH

(Abstracted from the *Journal of the American Medical Association*, Vol. 130, 13th April, 1946, p. 999)

EXPERIMENTAL studies on the fenestration operation in the monkey indicate that the following factors govern osteogenesis tending to close the fistula:

1. The sluggish response to trauma of the enchondral layer of the labyrinthine capsule.
2. The inhibiting effect of stratified squamous epithelium on osteogenesis.
3. The stimulating effect of bone dust and fragments on osteogenesis.
4. The stimulating effect on osteogenesis of trauma to the endosteum within the labyrinth.
5. The inhibiting effect on osteogenesis of a smooth polished bone surface.
6. The tendency of the intact membranous labyrinth closely adherent to the skin flap to hold the mouth of the fistula open.

By attention to all of the factors governing osteogenesis, using the 'nov-ovalis' fenestration technique with constant irrigation and the microscope, it has been possible for the first time to make a labyrinthine fistula in an experimental animal which has remained open for more than a year. With this technique the closures in the human patients have been reduced to less than 5 per cent after two years.

Clinical analysis of results in 930 consecutive fenestration operations over seven and one-half years indicates that osteogenesis tending to close the fistula is as a rule no longer active two years after operation.

The two-year hearing result of the fenestration operation may be regarded as the permanent result.

Antitoxic Action of Penicillin

(Abstracted from the *Journal of the American Medical Association*, Vol. 130, 13th April, 1946, p. 1017)

SUPPLEMENTING their earlier work with meningococcus endotoxin Miller and his associates of the University of Chicago Department of Medicine report that penicillin has an equally effective neutralizing action against gonococcus endotoxin. The endotoxin used in their tests was prepared from five strains of gonococcus grown for eighteen hours on an agar medium containing casein digest and cystine. The organisms were repeatedly washed in saline solution, suspended in distilled water and then allowed to autolyse for six hours at room temperature, followed by fourteen hours' storage at 4°C. The autolysate was then neutralized, heat sterilized (60°C. for thirty minutes) and its concentration adjusted to about 1 per cent solids. White mice weighing 18 to 20 gm. were injected intraperitoneally with graded doses (0.1 to 0.5 c.c.) of this 1 per cent endotoxin. Half of each group served as untreated controls. The other half were each given eight subcutaneous injections of 150 units of penicillin. The injections were usually given ninety and forty-five minutes before and one, three, five, nine, twenty and twenty-four hours after injection of the endotoxin. In a typical experiment 22 control mice were each injected with 0.1 c.c. of endotoxin. Of these, 15 died, a mortality rate of 68 per cent. Of 22 mice treated with penicillin similarly injected, only 2 died, a mortality of but 9 per cent.

Incidence of the Rh Factor

(From the *Journal of the American Medical Association*, Vol. 130, 13th April, 1946, p. 1046)

DR. HUMBERTO C. FERREIRA, Dr. Carlos S. Lacaz and Dr. Oswaldo Mallone of the Department of Microbiology and Immunology of the University of Sao Paulo have recently reported a study of the Rh factor in 260 white inhabitants of Sao Paulo using anti-Rh

serum furnished by the Blood Transfusion Association of New York. Of these, 222 were Rh positive (85.4 per cent) and 38 were negative (14.6 per cent). This result does not differ significantly from the findings of Landsteiner, Wiener, Tisdall and Garland in white populations. In 249 persons of known blood type the results were as follows: in 139 persons of type O there were 116 Rh positive (83.5 per cent) and 23 negative (16.5 per cent); in 92 persons of type A there were 85 Rh positive (92.4 per cent) and 7 negative (7.6 per cent); in 15 persons of type B there were 13 Rh positive (86.7 per cent) and 2 negative (13.3 per cent) and in 3 persons of type AB all were Rh negative. There was a significant difference between the two sexes: in 106 males there were 95 Rh positive (89.6 per cent) and 11 negative (10.4 per cent) and in 154 females there were 131 Rh positive (85.1 per cent) and 23 negative (14.9 per cent).

Post-Prandial Variation in Hæmoglobin

By A. W. BRANWOOD

(Abstracted from the *Edinburgh Medical Journal*, Vol. 53, March 1946, p. 125)

1. THE percentage of hæmoglobin in the peripheral blood is not constant throughout the day.

2. There is usually a post-prandial fall in hæmoglobin of the order of 5 to 10 per cent. This fall is in proportion to the size of the meal—the larger the meal the greater the fall. There is also, presumably, a fall in the number of R.B.C. at this time. It will be obvious that when periodic hæmoglobin values are required they should not be estimated within three hours following a large meal, or should be estimated at the same time of day, in order to avoid this post-prandial fall.

3. The possible cause of this decrease in hæmoglobin has been discussed. It is probably due to a redistribution of the cells from the periphery to the abdominal viscera and, possibly, also to slight changes in blood volume.

4. This fall in hæmoglobin can be prevented by exercise or by the administration of adrenalin.

5. Cases of hypertension and hyperthyroidism do not share this post-prandial decrease in hæmoglobin and further investigations are required on this subject.

Methods of Treatment of the Psychoses

By J. G. HAMILTON

(Abstracted from the *Medical Press and Circular*, Vol. 215, 22nd May, 1946, p. 342)

In the last 10 years or so a number of physical treatments have been introduced into psychiatry which few practitioners have had the opportunity of seeing, since they are carried out almost exclusively in mental hospitals.

It frequently happens that shortly after the admission of a patient to the hospital, the relative's consent to one of these treatments is requested, and before giving it, he often turns to his general practitioner for information about the treatment and its risks.

It is to assist the practitioner in this matter that the following short account has been written:

Electrical convulsion treatment is the method of inducing artificial epileptic fits by passing a current of electricity between the temples. This treatment is usually given 2 or 3 times weekly, and the number usually needed varies from about 5 to 20. The treatment is used for cases of depression or mania, for early cases of schizophrenia, for certain cases of anxiety states, hysteria and obsessional neurosis, and for confusional conditions.

The best results are seen in depression, and it is the treatment of choice for this condition if it is at all profound. Many authorities claim a recovery rate of 80 per cent of cases treated by this method.

Good results are seen in obsessionals, but relapses occur, and for these, leucotomy is often necessary. The results of electrical convulsion treatment in mania and in confusional states are also good. It is regularly used for the treatment of early cases of schizophrenia in all its forms, when insulin treatment is not available, and good results are obtained.

Electrical convulsion treatment is a severe physical strain, but is remarkably well tolerated, even by thin and weak patients. It is indeed surprising that the contra-indications to its use are so few.

The risks of treatment are the risks of injury during the convulsion. These are now very rare when care is taken to put the patient in the proper position before the current is passed. From their own muscular exertions, patients may tear muscle fibres and dislocate joints, or even fracture bones. Perhaps the commonest fracture is a crush fracture of the body of a vertebra.

The treatment imposes a severe strain on the heart, due to the exertion and to the congestion of its right side during the period of cyanosis, but very few instances of sudden heart failure have been reported.

One unpleasant symptom is the loss of memory for recent events which occurs while treatment is being given, but which usually disappears within a month of the last treatment. Some patients complain of being unable to remember phone numbers and dates which they had previously had no difficulty in recalling.

Continuous narcosis is a method of treatment in which, by the use of sedatives, the patient is kept in a state of sleep for most of the 24 hours for a period of 10 to 20 days.

It was of much use in the treatment of service cases which had developed acute psychotic states from the severity of their experiences under conditions of extreme stress and danger.

The techniques vary with different operators, but usually involve the use of somnifaine and paraldehyde. When the effect of the drugs is wearing off, the opportunity is taken for giving food and other necessary attentions and then further barbiturates are given.

There are certain risks associated with this treatment which cannot be carried out without a highly-trained staff on continuous duty.

Apart from the war use already given, it is most used in cases of mania and in cases of anxiety and agitated depression.

Insulin treatment is a method used almost exclusively for the treatment of schizophrenia. It consists in inducing and maintaining a state of hypoglycæmia for some hours daily for 5 or 6 days a week until 20 to 50 comas have been given. The method is to give an injection of insulin at 7-30 a.m. to the patient who must have had no food for 12 hours. Within 2 hours there is sweating; slowly drowsiness supervenes, and coma develops within 3 hours of the injection of insulin.

After a period of about 1 hour, this is interrupted by introducing glucose into the stomach by a nasal catheter; this normally results in the patient waking up in about 15 minutes.

The appropriate insulin dose is found by starting with 20 units and working upwards daily. It is common for those undergoing this treatment to put on much weight owing to their increased appetites.

There are considerable risks attendant on this treatment, and even with a highly-trained staff it is necessary for the doctor to be always at hand to give immediate intravenous interruption if any serious complication appears.

The treatment is usually finished by lunch-time each day, but those receiving it must be kept under observation all day in case they return to hypoglycæmia spontaneously—the so-called after-shock.

Modified insulin.—The modified insulin treatment has been found of use in treating certain anxiety states, including certain cases of war neuroses and depressions, and some obsessional cases, and also in states of exhaustion. In this treatment, doses of insulin varying from 10 to 60 units are given daily, and the patient is kept in a darkened room.

The dose is less than sufficient to produce a coma, and food is given in a few hours. The usual result of a few weeks of this treatment is that a stone or more in weight is put on, and there is an increase in physical well-being.

Leucotomy.—This is an operation in which the white fibres running posteriorly from the prefrontal area of the brain are cut by an instrument introduced through a trephine opening. Different surgeons use different instruments for cutting the fibres, and the operation is usually performed under evipan or pentothal anaesthesia, combined with a local anaesthetic. There is commonly very little shock from this operation, and in some cases, particularly in obsessionals, there are dramatic results. In others, the improvement appears more slowly.

The special advantage of leucotomy is the absence of strain upon the heart, and it can be used to treat depression occurring in patients with hypertension or cardiac disability. It has been successfully given to a man who had already had one retinal detachment and who might have been made blind by the strain of electrical convulsion treatment.

Congenital Abnormalities in Infants following Infectious Diseases during Pregnancy, with Special Reference to Rubella : A Third Series of Cases

By C. SWAN

and

A. L. TOSTEVIN

(Abstracted from the *Medical Journal of Australia*, Vol. 1, 11th May, 1946, p. 645)

In the course of the present investigation 56 infants and 2 fetuses were examined; 46 of them were found to have congenital malformations.

In 40 instances the mother had suffered from rubella in pregnancy; 36 of the infants and a foetus exhibited congenital defects. The abnormalities comprised 11 cases of deaf-mutism, 11 cases of deaf-mutism and heart disease, one case of deafness and heart disease, one case of deaf-mutism, heart disease and strabismus, one case of deaf-mutism, cataract and heart disease, one case of deaf-mutism and naevus, one case of speech defect and heart disease, one case of cataract and lack of closure of the foetal fissure, two cases of heart disease, one case of mongolism and heart disease, one case of microcephaly, one case of microcephaly and backwardness in development, one case of cleft palate, one case of *spina bifida occulta*, one case of heart disease and hypertrophic pyloric stenosis, and one case of spastic diplegia, hypertrophic pyloric stenosis, inguinal hernia and strabismus. In addition, in a further 18 of the foregoing cases microcephaly was also present. Four of the mothers had had German measles in the first month of pregnancy, 19 in the second month, 8 in the third month, 2 in the fourth month and one in each of the fifth, sixth and eighth months; in the remaining case the duration of pregnancy at the time of infection was not determined. In three cases in which the infant born subsequently was normal, the mothers had contracted the disease in the second, fourth and sixth months of pregnancy, respectively.

In two instances in which rubella was contracted less than a fortnight before conception the offspring were apparently normal.

The infectious diseases during pregnancy in the remaining 16 cases included eight cases of morbilli (two of the babies were abnormal), three cases of mumps (all babies had defects), two cases of varicella (one baby was malformed), two cases of herpes zoster (both babies exhibited abnormalities), and one case of scarlet fever (the baby was defective).

The pathogenesis of the anomalies is discussed in the light of the experiments of Stockard.

Urea as an Adjunct to Sulphonamide Therapy

By HARRY VESELL, M.D.

IRMA H. GROSS, M.D.

and

RALPH M. SUSSMAN, M.D.

(Abstracted from the *Jl. Lab. and Clin. Med.*, Vol. 31, No. 4, p. 444)

THE use of urea as an adjunct in treatment with sodium sulfadiazine is described. A cure of subacute bacterial endocarditis so treated, with prompt recovery, is reported. While penicillin is preferable in cases of subacute bacterial endocarditis due to alpha haemolytic streptococcus in infections where large doses of sulfadiazine are required, the use of urea as an adjunct may be of considerable aid.

Urea helps by (a) direct potentiation of sulfadiazine; (b) inhibition of antisulfonamide substances—para-aminobenzoic acid (Woods), 'P' factor (Green), or other causes of sulfonamide fastness; (c) increased solubility of sulfadiazine in the blood due to the presence of increased concentration of urea; (d) increased solubility of sulfadiazine in the urine with reduction of crystalluria and consequent renal damage following massive doses of sodium sulfadiazine; and (e) possible direct action of urea on the fibrin protectorate of the bacterial colonies in the endocardial vegetations by (i) promotion of digestion of fibrin by proteolytic enzymes (dilute solutions of urea, 2 per cent, may have such action; Ramsden) and (ii) being deterrent to coagulation of proteins.

This combined sulfonamide and urea therapy may be desirable in some cases resistant to treatment with penicillin.

A. B. R. C.

Occlusive Dressing for Tropical Ulcer

(From the *United States Naval Medical Bulletin*, Vol. 46, May 1946, p. 748)

DESERT sores and similar conditions respond best to an occlusive method of treatment. An adhesive plaster of paris dressing has proved successful in the treatment of this condition.

The dressing consists of a powder rubbed into the mesh of an open-weave bandage, as it would be for a prepared plaster of paris bandage. The powder is composed of plaster of paris 75 per cent and tragacanth powder 25 per cent, to which is added acriflavine powder to give a strength of 1 : 1,000. Other antiseptic such as gentian violet or sulphanilamide may be used. The powder must be thoroughly mixed and finely ground.

Indolent ulcers, which are frequently met, respond well to an application of silver nitrate and sealing with the patch.

The dressing has been used with success in the early vesicular stage of desert sores, early treatment of boils, in treatment of impetigo, and particularly in abrasions and minor wounds of the head and face. The dressing has been applied over small lacerations, and in all cases rapid healing has been obtained.

This method of treatment is extremely economical. It is comfortable, does not restrict movement, and there is no irritation of the skin.

Fulminating Septicæmia due to Staphylococcus Epidermidis

By C. C. SHAW *et al.*

(Abstracted from the *United States Naval Medical Bulletin*, Vol. 46, May 1946, p. 751)

THE occasional ability of staphylococci to produce septicæmia has long been ascribed to the *Staphylococcus*

aureus, the most potent pathogen of the genus staphylococcus. The albus strains of staphylococcus are considered to be of feeble pathogenicity and of little importance other than in mild suppurative conditions of the skin.

The existence of a species producing a porcelain white colour, yet distinct from the recognized *Staphylococcus albus*, was first described by Welch in 1891 and named *Staph. epidermidis albus*. The same organism was isolated by Gordon in 1903. It is described in more recent literature under the name of *Staph. epidermidis* by Bergey, by Kolmer and Boerner and by Topley and Wilson.

Since this genus is agreed to be of feeble pathogenicity and a habitant of normal skin, it is considered of interest to report here a fatal case of sepsis, with multiple brain abscesses, which was encountered recently in which the offending organisms was proved to be the usually innocuous *Staphylococcus epidermidis*.

In our patient the portal of entry to the blood stream may have been an abraded or infected clavus on the fourth toe of the left foot. The apparent duration of the fulminating septicaemia was not over 5 or 6 days. Clinically, in the terminal phase, the case resembled meningococcal meningitis with meningococcaemia. Differential diagnosis was established by bacteriological study of blood and spinal fluid cultures taken before death and by smear and culture of the lesions in the heart, brain and intestine at necropsy, all of which yielded a pure growth of *Staphylococcus epidermidis*.

Progress in Treatment of Subacute Bacterial Endocarditis

(From the *United States Naval Medical Bulletin*, Vol. 46, May 1946, p. 763)

THREE HUNDRED AND FORTY-SEVEN proved cases of subacute bacterial endocarditis treated at the Peter Bent Brigham Hospital from 1913 to 1945 were studied. There were no known recoveries among 237 cases seen between 1913 and 1937, during which time a great variety of therapeutic procedures was employed.

Of the 90 cases observed from 1937 to 1943, 55 received adequate treatment with a sulphonamide. Sixteen of the latter patients were given simultaneous fever therapy. Of these, one treated by infra-red radiation and three treated by typhoid vaccine recovered and have remained well for from 2 to 4 years. None of the other sulphonamide-treated patients recovered.

Of 20 patients studied since January 1944, 17 were given large doses of penicillin. In 11 cases the infection has been cured or arrested and the patients are now alive. The follow-up periods vary between 6 and

18 months. In two others the infection was bacteriologically arrested but death occurred some weeks later because of complications.

Soya Bean

(Abstracted from the *Current Science*, Vol. 15, June 1946, p. 158)

THE results of the co-ordinated investigations carried out in the four laboratories at Bombay, Coonoor, Dacca and Lahore, under the auspices of the I. R. F. A., have recently been published as a Special Report (I. R. F. A. No. 13).

The biological value and digestibility coefficient of the soya bean protein by growth and metabolic studies on albino rats and in human beings were found to be of the same order as those of the other pulses. In spite of its high available protein content (1½ to 2 times that of pulses) soya bean did not prove any better than the common Indian pulses as a supplement to the poor rice diet. In most experiments Bengal gram seems to have given better results than even soya bean. Incidentally it has been found that the so-called 'poor Madras' diet suffers more from a lack of minerals and vitamins than from that of proteins.

One of the methods of processing soya bean for human consumption is to prepare a milk-like fluid from it. Soya bean is softened by steeping for varying periods in warm water and is then ground with further addition of water. When coarse particles are removed by sieving an emulsified fluid is left behind. The emulsion thus obtained looks like milk and in composition varies according to (a) the method of preparation and (b) the quantity of water added. For ages 'soya milk' thus prepared has been used in China; the main reason for its extensive use in certain regions in China is the almost complete absence of cow's milk from the prevalent human dietary. The soya emulsion prepared as above is inferior even after fortification with salts and vitamins in nutritive value as compared with fresh whole milk. There could be no doubt that an emulsion from the germinated bean would give a preparation with a greater nutritive value as compared with that obtained from untreated beans. There is little proof, however, to show that it approaches cow's milk, although it may appear to be so by virtue of its chemical composition; this is a crude way of comparing two biologicals. The I. R. F. A. Report makes it clear that all the available evidence points to the conclusion 'that soya bean preparations, if fed to infants, need to be supplemented by minerals and vitamins and that even after such supplementation they are less satisfactory than breast milk or cow's milk'.

Reviews

PREVENTIVE MEDICINE.—By M. F. Boyd, M.D., M.S., C.P.H. Seventh Edition. 1945. W. B. Saunders Company, Philadelphia and London. Pp. x plus 591. Illustrated. Price, 27s. 6d.

The seventh edition of this book incorporates the current advances on preventive medicine, involving extensive changes in the volume. Those diseases and deficiencies whose causes are sufficiently well known and which are therefore more or less preventable have been dealt with in the book. Naturally the diseases caused by micro-organisms occupy a large part of it, and along with them are considered water, milk and other foodstuffs, and the parts they play in transmitting infection. The disposal of excreta is fully treated in two chapters with several illustrations. The section on nutrition has been practically rewritten in the light of recent concepts. Other subjects dealt with are occupational diseases, the puerperal state, heredity and disease, and hygiene of infancy and childhood. The

last two sections are on vital statistics and public health. The book presents salient features of preventive medicine with special emphasis on methods of control and with an eye on the sociological nature of the problems. It is a sound and well-balanced book.

R. N. C.

DISORDERS OF THE BLOOD: DIAGNOSIS, PATHOLOGY, TREATMENT AND TECHNIQUE.—By Sir Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. (Cantab.), F.R.C.P. (Lond.), D.P.H., and C. J. C. Britton, M.D. (New Zealand), D.P.H. Fifth Edition. 1946. J. and A. Churchill Limited, London. Pp. xii plus 665, with 15 plates (10 coloured) and 71 text-figures. Price, 30s.

THIS standard book has been thoroughly revised and brought up to date in every respect. Many changes have been made in the chapters on the origin and

development of the blood cells, the hæmolytic anæmias, the anæmias of infancy and childhood, hæmagglutination and blood transfusion. The text has been increased by sixty-two pages and some coloured illustrations have been included. The book provides a balanced and accurate account of modern knowledge on diseases of the blood, and is too well known to require recommendation.

R. N. C.

AN ATLAS OF THE COMMONER SKIN DISEASES.—

By Henry C. G. Semon, M.D. Third Edition. 1946. Pp. viii plus 343, with 139 plates in colour. John Wright and Sons Ltd., Bristol. Price, 25s.

ONE has nothing but praise for this book of 139 life-like portraits, in spite of its somewhat limited utility in India.

Descriptions of the diseases depicted in the plates create an atmosphere of a clinic where 139 cases are being shown and discussed. A few less common diseases, without which the book would have been incomplete, are also included. The treatment is complete and up to date, though brief.

Of special interest are the following items: (1) A case of Exfoliative Dermatitis developing Mycosis Fungoides. (2) Treatment of eczema with urinary protease. (3) Chronic Superficial Glossitis of latent syphilis with a weak or negative WR. (4) Unsuitability of sulphonamides for epidermal cells which are liable to be sensitized. (5) Abatement in chronic Sycosis Barbæ after replacement of ordinary razor by electric razor-scissors action. (6) Successful treatment of Pemphigus Vegetans with malaria.

The paper and printing are excellent. The binding could have been better. The price for a book of this type is reasonable.

S. D. S. G.

A POCKET MEDICAL DICTIONARY.—Compiled by L. Oakes. Seventh Edition. 1946. Pp. xx plus 430. E. and S. Livingstone Limited, Edinburgh. Price, 4s. net

SISTER OAKES has brought out a seventh edition of the dinky little dictionary she compiled thirteen years ago. It is a concise and compact pocket volume complete in all details, compatible with its size.

Paper, printing and binding are excellent. The price is moderate.

S. D. S. G.

A SHORT PRACTICE OF SURGERY.—By Hamilton Bailey and R. J. McNeill Love. Seventh Edition. 1946. H. K. Lewis and Company, Limited, London. Pp. viii plus 1097, with 1,063 illustrations of which 203 are coloured. Price, 40s. net

THE appearance of this new edition is most welcome for three reasons. Firstly, because it is a favourite and reliable text and everyone likes to see an old friend again. Secondly, because its appearance at this time gives renewed evidence of its vigour. Thirdly, because it is the only text containing an up-to-date assimilation to practice of the many proved advances which have taken place during this last war. The patient and persistent labour the authors have put into this work under the trying conditions prevalent in England during and since the war cannot be realized by the average reader, who, treated to a masterpiece such as this edition, is all too apt to demand more from where it came without thought as to what a labour of love the making of such a book is.

The contents, as always, are concisely accurate. The pictures speak more than any written paragraph. The historical references in the footnotes give the whole an enlivening culture sadly absent these days from the average surgical text.

This text should be in the hands of every medical student and practitioner. It cannot be absent from

the desk of the practising surgeon and teacher and would be a grave omission from the desk of the fellow-ship candidate.

A. T. A.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY.—By Hamilton Bailey, F.R.C.S. Tenth Edition, Revised. 1946. John Wright and Sons Ltd., Bristol. Pp. xii plus 375, with 573 illustrations, a number of which are in colour. Price, 30s.

THE number of coloured illustrations in this edition has increased to the enhanced usefulness of the book. Its slimness is welcome, for the beauty of this book lies in the fact that it gives the surgeon the meat of the classics on diagnosis in easily assimilable form. One is tempted to describe the accessibility of the contents in terms appropriate to these days of quick lunch counters and air travel by saying 'It's all on the plate' and it is full of 'Happy landings'.

This book and all Mr. Bailey's work are too well known to require recommendation. The names of Bailey and his publishers are synonymous with conciseness and accuracy, beauty of reproduction, in short a genuine work of art.

To the student, under-graduate and post-graduate seeking to equip themselves with a surgical library one can safely recommend a set of Hamilton Bailey's works.

A. T. A.

DISEASES OF THE SKIN. FOR PRACTITIONERS AND STUDENTS.—By G. C. Andrews, A.B., M.D. Third Edition. 1946. W. B. Saunders Company, Philadelphia and London. Pp. vi plus 937, with 971 illustrations. Price, 50s.

THIS useful book might as well be called an exhaustive atlas of skin disease in view of its 937 pictures which although only in black and white are excellent. Unusual items include 'Dermatitis from Chromium Wrist Watch' (on page 105).

The presentation of the subject though concise includes all details of anatomy, diagnosis, up-to-date treatment and prognosis. An advance in anatomy is the importance of the prickle-cell layer which in healing wounds gives rise to the basal layer (page 1). Unusual items include Occupational Leukoderma (on page 840) and Electrogalvanic Lesions of the Oral Cavity produced by metals and cements used in dentistry (on page 805).

Sections on physical therapy employed in Dermatology excel in brevity, clarity and utility anything the reviewer has seen in books of this size. One of them has been specially written by a radiologist.

Venereal diseases include Reiter's disease (page 281) and Behcet's Triple-symptom Complex (page 405). The chapter on syphilis has 88 pages and together with observations made elsewhere in the book (e.g. 'Anti-syphilitic treatment of leukoplakia of the tongue is undesirable' on page 807) gives a complete plan of diagnosis and treatment of the disease as a whole. In this otherwise valuable section two flaws have crept in, due probably to re-writing of the book: some pictures have been separated from the text (e.g. description of annular syphilis on page 426 but its picture on page 470) and others displaced altogether (e.g. figure 429 on page 471 is not one of a mucous patch described on page 424; figure 523 on page 490, referred to on page 429, is not one of juxta-articular nodules which are shown in figure 526, on page 492).

Re-writing is probably also responsible for the lack of orthodoxy in references: (1) Many of them are not found in the text. The list at the end of chapter 1, on page 13, has 20 references out of which only 2 are found in the text. (2) They are neither numbered nor alphabetically arranged. (3) As indicated by their titles, most of them constitute a bibliography really.

Tropical diseases have been included; Bejel, however, is missing.

The book has been offered, modestly, to practitioners and students. As a matter of fact it is a book for the

specialist in dermatology or a senior practitioner who is called upon to give an opinion, if not the details of treatment, in all cases not obviously surgical. The students, English or Indian under-graduates, will find it rather large, notwithstanding its readability.

The paper, printing and binding are good. No printer's errors attract attention. The price is not unreasonable.

S. D. S. G.

MEDICAL RESEARCH COUNCIL. INDUSTRIAL HEALTH RESEARCH BOARD. REPORT NO. 89. ARTIFICIAL SUNLIGHT TREATMENT IN INDUSTRY: A REPORT ON THE RESULTS OF THREE TRIALS—IN AN OFFICE, A FACTORY AND A COALMINE.—By Dora Colebrook. Published by His Majesty's Stationery Office, London. 1946. Price, 1s.

As a remedy for certain definite diseases, ultra-violet irradiation, or, as it is popularly called artificial sunlight treatment, has been widely used in medicine but it has also been recommended on less sure foundation, both as a general tonic and as a means of preventing or correcting minor conditions of ill health. It has been said that the black-out conditions that prevailed in Great Britain during the war years by depriving the workers of ultra-violet rays in natural sunlight, have aggravated the harmful effects which many of them feel that they suffer as a result of working in artificially lighted places; and this has encouraged the increased use of artificial sunlight as a prophylactic in industrial communities. It has been claimed that a course of ultra-violet exposures by promoting good health should have the effect of reducing absenteeism due to sickness, accidents, the common cold and general ill health. In view of the conflicting nature of the previous evidence on the subject the Medical Research Council organized a controlled and a large-scale enquiry which was carried out by Dr. Dora Colebrook under the direction of the Industrial Health Board. The trials were made in three separate communities in an office, a factory and a coalmine, most of them working entirely in artificial light. The results of these careful and extensive observations are given in this report and should be of interest to those practising this form of therapy.

R. N. C.

RYPINS' MEDICAL LICENSURE EXAMINATIONS: TOPICAL SUMMARIES, QUESTIONS AND ANSWERS.—By Walter L. Bierling, M.D., F.A.C.P., M.R.C.P. (Edn.) (Hon.). Fifth Enlarged Edition. 1945. Pp. xxii plus 546. Price, 36s.

This book is designed to assist students in examinations conducted by the medical registration boards of the U.S.A. and deals with ten subjects, viz, anatomy, physiology, chemistry, bacteriology, pathology, hygiene and preventive medicine, obstetrics and gynaecology, medicine, surgery and, added in this edition, pharmacology. On each subject a number of questions have been given, and these have been selected as being typical after a survey of many thousands of questions actually used in examinations. The questions are preceded by a brief review of that subject. Though not sufficiently comprehensive, they offer a fair ground for exercise on the eve of examinations. The reviews themselves are very limited in scope, each occupying on an average about 45 pages but, taken all together, they supply a surprising amount of information which will be found convenient for reference or as memory-quickener.

R. N. C.

CLINICAL DEMONSTRATIONS TO NURSES.—By Hamilton Bailey, F.R.C.S. (Eng.). Second Edition. 1946. Published by E. and S. Livingstone Limited, Edinburgh. Pp. 136. Illustrated (many in colour). Price, 10s. 6d.

This is an extremely useful textbook. The plates are beautifully clear and each demonstration is so

simply worded as to be easily understood by the most junior nurse. The demonstrator continually shows how the work of doctor and nurse can be co-related for the good of the patient. The use of surface Anatomy as shown in some of the plates should be much more commonly adopted in the education of nurses. This is a book which every teaching institution should have in its library. The price is extremely moderate for such an instructive publication.

P. B.

THEORY AND PRACTICE OF NURSING.—By M. A. Gullan, S.R.N. Fifth Edition. 1946. H. K. Lewis and Company, Limited, London. Pp. xii plus 236. Price, 12s. 6d.

This is an extremely useful book for a 'sister tutor's bookshelf' and (if used as Miss Gullan suggests in her foreword) to nurses; an excellent book for the senior nurse also. It is comprehensive and great attention is paid to detail. Particularly the reviewer liked the chapters on Pulse, Respiration, Temperature, Elementary Dietetics and Administration of Drugs.

The price 12s. 6d. is well within the reach of the second year nurse and the value is good.

P. B.

BOOKS RECEIVED

Nutrition. Bulletin No. 20, August 1946. Department of Food, Government of India, New Delhi.

Proceedings of the Seventh Annual General Meeting of the Tuberculosis Association of India held on the 27th March, 1946, at the Viceroys' House, New Delhi.

Seventh Annual Report of the Tuberculosis Association of India for the year 1945. Published by the Tuberculosis Association of India, New Delhi.

Convocation Address. Delivered on the 19th July, 1946. By The President, Lieut.-Colonel B. G. Vad, M.D., F.C.P.S. Published by College of Physicians and Surgeons of Bombay, Hospital Avenue, Bombay 12.

Abstracts from Reports

ANNUAL REPORT OF THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE FOR THE YEAR 1944-45

MANY of the happenings recorded in the report belong to a chapter of wartime activity happily ended. The courses of instruction for service medical officers have been discontinued and courses for the diploma in public health and for the diploma in tropical medicine are already in progress. Many changes in the staff were made during the year, including the retirement of Professor Greenwood from the department of epidemiology and vital statistics. In spite of wartime difficulties some useful work was done overseas, and several members of the staff were sent on special missions. An outstanding event of the year was the gift of over £20,000 from the Rockefeller Foundation for the training of picked men in public health. A small amount of research has been conducted on anti-malarial drugs received from the U.S.A. One of these, diquinin, still on trial, promises well in the treatment of carriers of *E. histolytica*.

The reports of many of the departments of the School indicate extensive field work. Investigations on onchocerciasis in Kenya and a helminthological survey in Northern Rhodesia were completed, and much work has been done on insect physiology and insecticides, tsetse flies and trypanosomiasis, control of bugs, flies and cockroaches, etc. Important advances have been made in the protection of the soldier in the tropics

from biting insects and from the diseases which they transmit. Various uses of DDT are being investigated. By the way, it was found that domestic dusting or washing causes a great reduction in the insecticidal effect of DDT films. Work was also undertaken on the ventilation of ammunition factories where the dusts and fumes not only caused discomfort but endangered the lives of the operators.

R. N. C.

THE ROCKEFELLER FOUNDATION : THE REVIEW FOR 1945

THE Rockefeller Foundation concerns itself with the 'well-being of mankind throughout the world', yet it is an irony of fate that it played a part in—an unwilling part—in the creation of the atomic bomb, in as much as a number of leaders of the project had received part of their specialized training on fellowships provided by Rockefeller funds. But, of course, when the various grants were made, no one was thinking of the atomic bomb. However, the good work for which it has become famous continues, and a review of the work done in 1945 shows that over eleven million dollars were appropriated for various purposes, 64 per cent of which was spent in the U.S.A. and 36 per cent in other countries. The grants covered projects ranging from development of a Russian Institute for better understanding of Russia to animal husbandry in Iceland. But its notable achievement was the eradication of *Anopheles gambiae* from upper Egypt which it had invaded in 1942 from the African tropical belt, causing the most serious epidemic of malaria in the history of that country. The largest grant made in 1945 was a million dollars to Harvard University for its school of public health. Other grants were for the teaching of far eastern languages and culture, agricultural researches in Mexico, psychiatric work, etc. The Foundation helped many European refugee scholars since 1933, but the work has now ended. In the last 30 years it has given fellowships to about 7,700 men and women from 72 different countries. This programme which was necessarily curtailed by the war will be restored as soon as possible. Referring to a grant to Dr. Weidenreich of New York Natural History Museum, the report mentions that he has been able to construct, on the basis of some fossil bones and teeth, his hypothesis of a genus of early man, not only more primitive than any hitherto identified, but huge in size. Incidentally, the loss is reported of the skull fragments and teeth of Peking Man (who lived probably 500,000 years ago), while being sent away from Peking at the time of Pearl Harbour.

R. N. C.

Correspondence

'SULPHAPYRIDINE AND SULPHATHIAZOLE AS HELMINTHAGOGUE'

SIR,—It is not uncommon to see patients, of all ages, but mostly between 3 and 18 years, with sallow dry and harsh skin, with thin emaciated and anæmic facies. These persons appear with distended abdomen and usually complain of occasional pain in abdomen and other gastro-intestinal disturbances, and of voracious appetite. Their chief complaint is 'Bloodlessness and occasional abdominal pain'. In the majority of cases, I have noticed that salivation is the chief trouble.

I happened to treat the patients of the above type for pneumonia, gonorrhœa, tonsillitis and other inflammatory conditions, wherein I used sulphapyridine and sulphathiazole. I was surprised to see that in three cases dead roundworms (in 2 cases) and in one hookworms were passed. I attempted the same treatment in 4 cases, which were established cases of ankylostomiasis. It was rather encouraging to note that these

4 patients passed out worms, though in one case it was rather suspicious.

Yours, etc.,
B. B. RAI, M.B., B.S., R.S.,
Divisional Surgeon,
St. John Ambulance.

BAREILLY, U. P.,
29th July, 1946.

N.B.—Sulphapyridine and sulphathiazole were used with nicotinic acid tablets and celin with glucose.

HAIR ON THE INDEX FINGER

SIR,—I shall be obliged if you publish a piece of observation which seems to me to be very interesting.

The skin over the dorsum of 'Little', 'Ring' and 'Middle' fingers of both the hands shows hairs on the first and second phalanges. The skin on the thumb on the first phalanx also shows hairs. The skin on the first phalanx of the index fingers shows hairs as usual but I have never come across hairs on the skin on the second phalanx of the index fingers. This is very perplexing. In some individuals no hairs could be seen on the skin of the second phalanges of 'Little', 'Ring' and 'Middle' fingers but even when they are present the index fingers, so far as my observation goes, do not show any growth of hair. I have observed this on about 50,000 persons. I have searched all the locally available literatures but I find no mention about this.

Yours, etc.,
D. M. GUPTA,
Curator, Pathology Museum,
Medical College, Calcutta.

[A random sampling in the office of the *Indian Medical Gazette* showed three subjects (out of a total of 10) with hair on the dorsal surface of the second phalanx of the index finger of both hands.—EDITOR, I.M.G.]

Any Questions

ACTION OF SULPHA GROUP OF DRUGS ON PREGNANT UTERUS

SIR,—Would you kindly ascertain and publish what action the sulpha group of drugs has on the pregnant uterus? Recently abortion took place after administration of 24 tablets of one of the preparations of these drugs. The usual causes of abortion were apparently excluded in this case. Perhaps someone with facilities would like to investigate if it has not already been done.

Yours, etc.,
S. C. SEN,
Ex. Deputy Surgeon-General, Bengal.

[These drugs by themselves have got no *ecbolic* action. But very often the febrile or septic condition for which these drugs are rightly or wrongly prescribed does cause abortion. Occasionally the methæmoglobinæmia caused by the uncontrolled use of these drugs has been known to cause retroplacental hæmorrhage and that has led to abortion. Cases have been reported where the defective excretion of these drugs has led on to complete or partial anuria and this in pregnant condition indirectly leads on to abortion. Recently I came across a case of probable agranulocytosis leading on to grave oral sepsis. This caused a severe aspiration pneumonia—the patient aborted and then died. There are instances of wrong and careless use of the drug leading to abortion. I know of no single case of abortion after proper therapeutic use of this valuable group of drugs.—M. S.]

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL A. H. HARTY, C.I.E., V.H.S., is appointed Honorary Physician to the King, with effect from 23rd August, 1945, *vice* Major-General W. C. Paton, C.I.E., M.C., retired.

Major E. A. O'Connor, an Agency Surgeon, is employed as Chief Medical Officer in the Western Indian and Gujrat States Agencies and Residency Surgeon, Rajkot, with effect from the forenoon of the 2nd March, 1946.

Lieutenant-Colonel W. T. Taylor, Deputy Assistant Director-General (Medical Stores), Medical Store Depot, Bombay, is appointed Officer on Special Duty in the Office of the Director-General, Indian Medical Service, with effect from the 20th May, 1946.

Major E. A. R. Ardeshir is appointed to be the Superintendent of Presidency Jail, with effect from the 8th June, 1946, until further orders, *vice* Lieutenant-Colonel S. L. Patney, I.M.S. (retired).

LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commission)

To be Lieutenant

Charles Richard Peck. Dated 5th March, 1943.

LEAVE

Lieutenant-Colonel C. A. Bozman, O.B.E., Additional Public Health Commissioner with the Government of India, was granted leave *ex-India* for 6 months, with effect from the afternoon of the 2nd May, 1946.

Lieutenant-Colonel S. L. Patney, I.M.S. (retired), Superintendent, Presidency Jail, is allowed leave for 4 months, with effect from 8th June, 1946, the date of termination of the period of his re-employment.

PROMOTIONS

Captains to be Majors

W. J. Young, M.B.E., D.S.O. Dated 1st February, 1946.

J. L. Mewton. Dated 1st March, 1946.

J. F. Thomson. Dated 17th March, 1946.

E. J. Crowe, O.B.E. Dated 23rd April, 1946.

LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Lieutenant to be Captain

C. R. Peck. Dated 5th March, 1944.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

Lieutenants to be Captains

Miss B. E. M. Judson. Dated 11th January, 1946.

Miss M. Leahy. Dated 19th May, 1946.

RELINQUISHMENTS

The undermentioned officers are permitted to relinquish their commissions on release from Army Service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Major V. D. Nimbkar. Dated 11th March, 1946.

Major Mohd. Arshad. Dated 25th April, 1946.

Major V. P. Patel. Dated 4th May, 1946.

The undermentioned officer is permitted to relinquish his commission on grounds of ill health :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

Captain D. B. Parakh. Dated 16th April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from Army

Service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Captain Krishnadhan Banerjee. Dated 15th January, 1946.

Captain (Mrs.) E. H. Johnson (*née* Adelphus). Dated 20th March, 1946.

Captain W. G. Anderson. Dated 13th April, 1946.

Captain M. R. Juneja. Dated 25th April, 1946.

Captain E. L. C. Pushong. Dated 26th April, 1946.

Captain T. T. Ramalingam. Dated 9th May, 1946.

(WOMEN'S BRANCH)

Captain Miss P. B. Bellhart. Dated 26th April, 1946.

RESIGNATIONS

The undermentioned officers are permitted to resign their commissions :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

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Captain S. N. Venkatakrishnan. Dated 4th April, 1946.

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(SHORT SERVICE COMMISSION)

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Original Articles

THE COMPARATIVE VALUE OF SOME METHODS OF TREATMENT IN CASES OF TROPICAL ULCER

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Hoogrijan P. O., Assam

Introduction

THE present state of our knowledge regarding the treatment of tropical ulcer (naga sore) is very unsatisfactory. A search of the literature available to me reveals very few series of controlled treatments and many of the claims made for various methods of treatment have not been substantiated by subsequent workers in this field. Moreover, the existence of many different methods of treatment of any one disease can usually be safely taken as an indication that none of them is really satisfactory.

Two opportunities have come my way recently. One is the presence of an epidemic of tropical ulcer in a group of tea estates under my medical charge; the second is the fact that supplies of penicillin are now freely available. The occasion has, therefore, been favourable for a large-scale experiment in treatment and, as the population under experiment is subject to some degree of discipline, it has been possible to carry out several series of parallel treatments under controlled conditions.

All the ulcers treated and recorded in this paper agreed with the usual description of the acute tropical phagædenic ulcer, and in every case where smears from the floor of the ulcer were examined, fusiform bacilli were found. The cases comprise all cases of tropical ulcer on five estates whose treatment commenced during the period 15th May, 1946 to 15th June, 1946. On each estate at least three methods of treatment, including penicillin, were used and no conscious selection of cases for any particular line of treatment was made. The number treated with penicillin was comparatively small because the drug is expensive and I was not in a position to advise extensive use of it until proof of its efficacy was forthcoming.

Previous References to Treatment

A search through the available literature reveals the following papers in which the period required for complete healing by various methods of treatment is recorded.

Corkill (1939) treated 28 'recent' cases with daily dressings of cod-liver oil combined with oral administration of one capsule of vitamin A concentrate daily. His control series of 30 similar cases received no vitamin concentrate and were not dressed with cod-liver oil. Most of this series were dressed with

'Zipp'. The average time taken to heal the vitamin group was 45 days and that for the other group was 39 days, the average healing rate *per diem* being 0.26 mm. in each series.

Bharucha (1943) used two methods of treatment. Treatment I involved daily dressing with 1/150 copper sulphate solution till the slough disappeared, followed by 40 per cent cod-liver oil in vaseline under elastoplast. Treatment II consisted in daily dressings with a powder containing 50 per cent sulphanilamide and 50 per cent iodoform followed by bi-weekly dressings with red lotion. Of those healed by treatment I, the average times taken were:—

Under one inch	.. 35 days
One to two inches	.. 46 days
Over two inches	.. 54 days

The cases under treatment II included those originally on that treatment together with the failures from treatment I. In the latter case, only the number of days on treatment II has been included in the calculation. The average times taken were:—

Under one inch	.. 20.7 days
One to two inches	.. 28.6 days
Over two inches	.. 31.3 days

Panja and Ghosh (1944) recommended removal of the slough with hydrogen peroxide followed by normal saline compresses changed every hour during the day, combined with daily bathing in 1/5,000 Condy's fluid and a nightly dressing with a powder of equal parts boric acid and sulphathiazole or sulphanilamide. When the ulcer was clean it was dressed twice daily with 0.5 per cent acriflavine ointment. Even with this elaborate and time-consuming method of treatment healing of their cases took 21 to 42 days.

Pattanayak (1944) recorded his results with a number of different methods of treatment but most of his individual series were small and he does not make quite clear exactly what periods elapsed between the commencement of treatment and complete healing. The average time appeared to be about 40 days.

Marsh and Wilson (1945) used occlusion by plaster of paris combined with a variety of local dressings, of which they preferred bipp and zipp ointments and powdering the ulcer with a thin layer of crystals of potassium permanganate. They report that 'of 85 cases, 59 were completely healed in an average time of just over 2 weeks'. Actually, a study of their figures shows that the average period of healing was 5.6 weeks (39 days) and that, even of those 49 which were healed in less than ten weeks, the average period of healing was 4.5 weeks (31.5 days).

Rao *et al.* (1945) used a complicated method involving cleaning of the ulcer under anaesthesia with a special preparation and dressing with another special preparation. They say that 'in less than three weeks the small ulcers were

almost healed and the large ulcers showed considerable improvement'. This suggests that their average period of healing would be not less than 30 to 35 days.

Brecher (1946) adopted an occlusive treatment using adhesive plaster changed once weekly, combined with weekly injections of neoarsphenamine and bismuth subsalicylate. The average time required for healing was 42 days, 85 per cent being healed within 60 days.

It seems that a fair average for all these different observers, using such a variety of treatments, would be not less than 35 days and probably longer.

Panja (1945) treated one case only with penicillin, using the drug as a wet dressing in a strength of 100 units per c.c. Four days on this solution produced clean granulation tissue and the penicillin was then discontinued. The sore healed up within seven days. This is the only reference I have been able to find to the use of penicillin in the treatment of this disease.

Present series of cases

The number of cases dealt with in the present investigation was 265, of which 86 were less than one inch in diameter, 66 were over one inch in diameter (all these cases were single ulcers) and 113 were cases with multiple (*i.e.* more than one) ulcers. The proportion of cases with more than one ulcer is strikingly high and seems to be a feature of the present epidemic.

The following methods of treatment were adopted :—

(a) Daily dressing with a compress of saturated mag. sulph. solution until the ulcer was clean, followed by daily dressing with cod-liver oil.

(b) Similar daily dressing with mag. sulph., followed by daily dressing with sulphonamide powder dusted on dry.

(c) Daily dressing with a compress of copper sulphate solution 1 in 150 in water until the ulcer was clean, followed by daily dressing with a 1 in 1,000 emulsion of acriflavine in sterile liquid paraffin.

(d) Daily dressing with a paste containing copper sulphate and phenol in glycerine—James' modification of McGuire's treatment (James, 1938)—followed by daily dressing with dry sulphonamide powder.

(e) Intramuscular injections of penicillin combined with daily dressing of the ulcers with cod-liver oil. In 12 cases the amount of penicillin given was 200,000 units spread over 48 hours (three-hourly injections). In the remaining 53 cases the amount given was 100,000 units administered in five three-hourly injections: between 9 a.m. and 9 p.m. No use was made of local dressings with penicillin solution in this series as information was wanted as to how far the supposed circulatory stasis

postulated by so many authors would or would not interfere with the action of penicillin.

(f) Three injections of neoarsphenamine at five-day intervals combined with local cod-liver oil under an occlusive dressing of elastoplast, changed at five-day intervals. Only three cases were treated by this method as the experiment was only designed to show that neoarsphenamine has no action on the fusiform bacillus.

In all cases the method of treatment selected was rigidly adhered to until at least 47 days had elapsed when the case was considered a failure as regards that particular method. After the forty-seventh day the treatment was either changed or adhered to according to the clinical condition of the case. The period of 47 days was arbitrarily selected because it was intended to review the results of treatment on the 31st July and any case admitted on 15th June and still unhealed on 31st July would have been under treatment for 47 days. Moreover, it was considered that since the average period required for healing reported by previous authors was in the region of 30 to 35 days, any ulcer which was not healed in 47 days must be considered as having benefited very little, if at all, from the particular treatment adopted.

No case was considered healed until epithelialization was complete, leaving a firm scar with no scab, the patient being considered fit to resume work immediately in the tea garden.

The results of treatment by each particular method are tabulated below :—

Clinical types	SUCCESSFUL IN 47 DAYS		UNSUCCESSFUL	
	Number	Average number of days to heal	Number	Per cent
(a) <i>Mag. sulph. and cod-liver oil. Total number of cases 59</i>				
Under 1"	24	24.8	6	20.0
Over 1"	6	35.3	5	45.5
Multiple	11	28.5	7	38.9
TOTAL ..	41	27.3	18	30.5

Note.—Very nearly one-third of this series showed little response to treatment; in those who did, the average time required for treatment was a fraction under four weeks.

(b) *Mag. sulph. and sulphonamide powder. Total number of cases 70*

Under 1"	9	24.7	6	40.0
Over 1"	13	31.5	6	31.6
Multiple	22	33.1	14	38.9
TOTAL ..	44	30.9	26	37.1

Note.—More than one-third of the cases must be regarded as failures and in those which were favourably influenced by the treatment, the average period needed was about four and a half weeks.

(c) *Copper sulphate and acriflavine. Total number of cases 35*

Under 1"	8	29.6	2	20.0
Over 1"	2	27.5	3	60.0
Multiple	16	29.8	4	20.0
TOTAL ..	26	29.6	9	25.7

Note.—In this series failures amounted to only just over one-quarter of the total but the average period of treatment required in those that responded was four and one-quarter weeks.

(d) *Copper sulphate paste and sulphonamide. Total number of cases 33*

Under 1"	16	29.1	2	11.1
Over 1"	2	22.5
Multiple	11	29.3	2	15.4
TOTAL ..	29	28.7	4	12.1

Note.—The proportion of failures in this series was much lower, in fact the lowest in all the groups tested, but the average period of treatment required remains at a fraction over four weeks.

(e) *Penicillin and cod-liver oil. Total number of cases 65*

Under 1"	11	26.7	2	15.4
Over 1"	22	24.5	4	15.4
Multiple	17	20.7	9	34.6
TOTAL ..	50	23.7	15	23.0

Note.—The proportion of failures is still high, just under one-quarter, but the period of treatment required in those cases which were favourably influenced has been cut to a little over three weeks.

(f) *N.A.B. and cod-liver oil under elastoplast*

Only three cases were treated by this method. All were single ulcers over one inch in diameter; two, 66 per cent, were failures; the single case which responded required 25 days.

Discussion

It has been shown by previous observers that the bacteriology of these ulcers bears a close relation to their clinical condition and that, as the ulcer becomes clean and acquires a healing edge, fusiform bacilli disappear from smears made from the base of the ulcer. Conversely, when an ulcer which has previously been found to contain large numbers of fusiform bacilli produces smears containing little or no fusiform bacilli, speedy healing can be expected. In two of the cases treated with N.A.B. there was no alteration in the smears until after the treatment had been changed and in the other the smears did not alter until after the third injection. These findings support an impression I had gained previously on clinical grounds that

Vincent's organisms are not affected by anti-syphilitic treatment.

Within the scope of this experiment penicillin may be said to have exerted a favourable influence on the healing of the ulcers. The proportion of failures was, with the exception of the rather small copper sulphate paste group, lower than under any other form of treatment and the average time required for healing was the lowest in the whole series. Actually, the results were disappointing because microscopical examination of smears repeatedly showed complete, or almost complete, absence of fusiform bacilli within 24 hours of the last injection of penicillin. This finding would justify one in the belief that rapid healing would follow and, in one case which I dressed myself entirely, such rapid healing did follow. Moreover, at two hospitals where numbers under treatment were not great and the staff were able to take greater care the results were consistently better. I am therefore reluctantly driven to the belief that many of these cases were to some extent re-infected during their treatment and the cod-liver oil had not sufficient antiseptic effect to deal with the re-infection.

For this reason I have recently started combining parenteral penicillin (95,000 units in 12 hours) with daily dressings for five days of gauze soaked in penicillin solution (500 units per c.c.) and following this with daily dressing with scarlet red ointment. The results so far appear to be good but it is too early to draw valid conclusions.

The very definite predilection of tropical ulcer for the lower third of the leg has been explained by an assumption that there is a slowing of the circulation in this area. This assumption has always seemed to me unnecessary as the site selection can be adequately explained on other (epidemiological) grounds. It is, therefore, interesting to note the speed with which a foul, offensive ulcer, full of felted slough containing myriads of fusiform bacilli, becomes clean and apparently sterile after intramuscular injections of penicillin. Having once seen this happen one would rather be inclined to say that these ulcers had a particularly good blood supply.

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CRUDE AND REFINED LIVER EXTRACT IN NUTRITIONAL MACROCYTIC ANÆMIA*

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TROPICAL macrocytic anæmia, as described by Wills (Wills and Mehta, 1930; Wills, 1934), now known as 'Nutritional Macrocytic Anæmia' (N.M.A.), occurs all over the world, and is commonly recognized as being due to multiple nutritional deficiencies. It is diagnosed as such if the patient has a blood picture typical of macrocytic anæmia and free hydrochloric acid, and if pepsinogen and rennin are present in the gastric juice. In pernicious anæmia (P.A.), free hydrochloric acid, pepsinogen and rennin are not secreted even after histamine injection. Macrocytic anæmias of sprue, pellagra and pregnancy are examples of N.M.A. with different pathogenesis.

Wills, Clutterbuck and Evans (1937) stated that the N.M.A. produced in monkeys by deficient diets and regarded as the animal counterpart of N.M.A. in man was not affected by refined liver extracts (by the insoluble fraction of the ammonium sulphate precipitate of whole Camplon or by Anahæmin). Later, Wills and Evans (1938) reported that N.M.A. in man in India was likewise unaffected by Anahæmin or similar highly-purified liver extract preparations. Napier *et al.* (1938) found Anahæmin effective in a group of N.M.A. but not in all. They suggest that N.M.A. is not a single entity and has no specific ætiology. Foy and Kondi (1938) and Fairley (1940) reported that N.M.A. responded well to Anahæmin, but these workers used Anahæmin in much larger dosage than was used by Wills or by Napier. Fairley (1940) concludes that if Anahæmin has to be given in larger dosage and possesses no advantage over the crude liver extracts given parenterally, its administration becomes prohibitive, on the grounds of expense alone, in the routine treatment of N.M.A. Trowell (1943) reported good results in six cases of N.M.A. with 12 c.c. weekly of Anahæmin, and Sundaram (1944) in 13 out of 15 cases with a total dosage of 12 c.c. of refined liver extract (Anahæmin, B.D.H., Examen, Glaxo or Reticulogen, Lilly). Moore *et al.* (1944) successfully used refined liver extract (Reticulogen, Lilly) in 25 cases of N.M.A. of pellagra.

Lately the following liver extracts were given to us for clinical trials: 1. Chemhepar (Chemo-Pharma); 2. Chemilon (Dr. Rao's Laboratory); 3 and 4. Plexan and New Potency Examen (Glaxo). These liver extracts were all found to be effective in the treatment of N.M.A., Plexan and Chemilon giving the better results.

The object was to find out the smallest quantity of crude liver extract necessary to produce optimum response and to show that the refined liver extract Examen in small doses—smaller than hitherto reported—does produce optimum response.

Material and method.—All the cases of anæmia studied according to the procedure adopted by us (Bhende and Patel, 1946) were those of macrocytic anæmia with presence of free hydrochloric acid in gastric juice and with a blood count below 3.0 million red blood cells per c.mm. The patients were given plain milk diet during the first fortnight and later vegetarian or such mixed diet as the hospitals provided. On this hospital diet (both milk and full diet) no hæmatological improvement occurred in any case at the end of 20 days. Hence we concluded that diet was not responsible for cure in any of the cases. When the patients were kept on milk diet, the œdema improved earlier than when given vegetarian or mixed diet. If after improvement, a patient with œdema was given a vegetarian or mixed diet, the œdema tended to return, while it disappeared quickly if the patient was restricted to a milk diet alone.

Besides the hospital diet, these cases of N.M.A. were given an alkaline gentian mixture if the gastric analysis (g.a.) showed normal HCl, and an acid mixture if there was hypo-acidity. No iron was administered. Vitamins of B-complex series were given to some of the patients by mouth or by injection.

Della Vida and Dyke (1942) have published the criteria for an optimum response from their extensive experience in testing liver extract in over 200 cases of P.A. and evolved the following formula:—

$I = 0.93 - 0.214 E_o$ where 'I' is the average weekly increase in red cells during the first two weeks of treatment and 'E_o' is the red cell count before treatment.

This formula, found to express what they consider a satisfactory response to treatment, is proposed by them as a standard equation for the assessment of the potency of liver extracts. The effectiveness of the liver extracts in the cases quoted here has been assessed by the above formula.

All the blood counts reported were done by the writer personally. Sternal punctures and smears were examined by Dr. Bhende, to whom my thanks are due. Routine stool, urine and gastric analyses were done by the central clinical laboratories. In none of the cases reticulocyte counts could be done for want of time. Murphy (1933) is of the opinion that the increase in erythrocyte is a better method of the assessment of the potency of liver extracts.

We have found before (unpublished observations) that Plexan liver extract proved effective when given in the dosage of 4 c.c. daily for 10 days, total 40 c.c.; also 2 c.c. daily for 10 days, total 20 c.c. It was also found to be effective

* Read before the 8th Maharashtra and Karnatak Provincial Medical Conference, held at Bijapur in May 1946.

when given as 10 c.c. daily for first 4 days. Under this massive depot method, improvement continued for a period of 40 to 60 days. This method has the advantage of reducing the period of stay in the hospital. Two cases where 2 c.c. were given daily for 6 days, a total of 12 c.c. are reported below :—

1. A male, aged 32 years, was admitted on 1st March, 1946, for general weakness, frequency of stools with mucus, and low fever of 2½ months' duration. He had puffiness of the face and œdema of the legs and was pale and emaciated.

G.A. (oatmeal) showed achlorhydria, but after an alcohol meal and histamine injection secreted acid. Stool examination showed presence of *Entamœba histolytica*. He was treated with sulphathiazole and kaolin powder and emetine injections, with the result that the frequency of stools lessened. He was then given an acid mixture. His blood count on 10th March, 1946, was 2.2 million rbc and 8.65 grammes Hb. He was given Plexan 2 c.c. daily for 6 days. In 14 days his blood count had risen to 3.96 million rbc and 11.76 grammes Hb. Improvement was very rapid and more than the optimum requirement. The anæmia in this case was due to deficient dietetic intake—the diet consisting mostly of starchy food and poor absorption, because of the chronic amœbic infection.

2. A man, aged 20, was admitted for general debility experienced for 2 months, diarrhœa and vomiting for 1½ months, pain in abdomen and sore mouth for 2 months. He was pale and emaciated. G.A. (oatmeal) showed achlorhydria, but after an alcohol meal and histamine injection secreted free HCl. Stool disclosed the presence of vegetative forms of *Entamœba histolytica*. Blood count on 25th March, 1946, was 1.48 million rbc and 5.19 grammes Hb. Plexan was given 2 c.c. daily for 6 days. On 13th April, 1946, blood count was 3.4 million rbc and 9.51 grammes Hb., which meant an optimum response in 19 days. Anæmia in this case was also due to deficient and mainly carbohydrate food which he was taking on account of abdominal pain and flatulence which in turn was caused by amœbiasis.

The following two cases were treated with Chemilon :—

1. A man, aged 45, admitted for general weakness for 4 months and giddiness and breathlessness on walking. He was markedly pale and had puffiness of face and œdema of legs. On examination of the central nervous system there was no abnormality. G.A. showed achlorhydria even after histamine injection. Stool examination revealed presence of ova of *Trichuris trichuria*, *Giardia lamblia* and cysts of *E. coli*. The sternal marrow showed erythroblastic-megaloblastic reaction with predominant erythroblast. Hence the diagnosis of N.M.A. Blood count on 14th April, 1946, was 0.88 million rbc and 3.70 grammes Hb. He was given 1 c.c. Chemilon daily for 8 days—a

total of 8 c.c. Blood count on 1st May, 1946, was 2.32 millions rbc and 7.26 grammes Hb., which was an optimum improvement.

2. A man, aged 40, suffering from N.M.A., was given 1 c.c. Chemilon for 8 days; blood count on 1st May, 1946, was 1.08 millions rbc and 3.76 grammes Hb.; blood count on 23rd May, 1946, was 2.2 millions rbc and 7.09 grammes Hb., which was a suboptimal response.

We had observed before (unpublished observation) that New Potency Examen was effective in small doses of 1 c.c. in cases of P.A. and also in cases of N.M.A. when given in dosage of 6 to 12 c.c. But in smaller dosage it was found to produce response in the following cases :—

1. A male, aged 22 years, with a history of chronic relapsing malaria 6 months, general weakness 4 months, breathlessness on exertion 1 month and occasional attacks of diarrhœa during the last 6 months; pale, slightly emaciated; spleen and liver just palpable. G.A. showed presence of free acid. Stool : vegetative forms of *Entamœba histolytica* and *Trichomonas hominis*. He was given the usual dosage of mepacrine for 5 days. On 4th December, 1945, his blood count was 1.0 million rbc and 3.76 grammes Hb. He was then given 1 c.c. of New Potency Examen for 3 days—a total of 3 c.c. Blood count at the end of 12 days was 2.68 million rbc and 8.40 grammes Hb., and in 7 days more, i.e. 16 days after his injections, it had risen to 3.76 million rbc and 10.38 grammes Hb. These 3 c.c. of Examen produced more than an optimum response.

2. A male, aged 45, suffering from anæmia and general debility of about 3 months' duration, had two years previously been admitted for N.M.A. His blood count on 26th February, 1946, was 1.84 million rbc and 8.40 grammes Hb. He was given 1 c.c. Examen daily for 3 days and at the end of 3 weeks his blood count was 3.72 million rbc and 12.11 grammes Hb. Here also there was a more than optimum response.

In both these cases 3 c.c. of New Potency Examen produced optimum response.

3. A male, aged 45, suffering from general debility and looseness of bowels, breathlessness and giddiness, showed free acid on G.A. His blood count on admission was 1.09 million rbc and 3.84 grammes Hb. He was given Examen 1 c.c. for 2 days—a total of 2 c.c. Fourteen days later his blood count was 2.24 million rbc and 7.78 grammes Hb. Improvement was good but slightly less than optimum.

4. A man, 22 years old, suffering from N.M.A., was given 1 c.c. of Examen when his blood count was 1.82 million rbc and 7.95 grammes Hb. Seventeen days later it increased to 3.08 million rbc and 10.38 grammes Hb. In this case 1 c.c. produced slightly less than an optimum response.

The responses to treatment in the eight cases described above are shown in the table appended.

Table showing response of 8 cases of N.M.A. to the different liver extracts

Number	Initial rbc in million	Initial Hb. in gm.	Final rbc in million	Final Hb. in gm.	Days	Dosage	REMARKS
I	2.2	8.65	3.76	11.76	14	2 c.c. × 6 days Plexan (12 c.c.)	Optimum response.
II	1.46	5.19	3.4	9.51	19	2 c.c. × 6 days Plexan (12 c.c.)	Optimum response.
III	0.88	3.70	2.32	7.26	16	1 c.c. × 8 days Chemilon (8 c.c.)	Optimum response.
IV	1.08	3.76	2.2	7.09	22	1 c.c. × 8 days Chemilon (8 c.c.)	Suboptimal response.
V	1.00	3.76	3.76	10.38	16	1 c.c. × 3 days Examen (3 c.c.)	Optimum response.
VI	1.84	8.40	3.72	12.11	21	1 c.c. × 3 days Examen (3 c.c.)	Optimum response.
VII	1.09	4.84	2.24	7.78	14	1 c.c. × 2 days Examen (2 c.c.)	Slightly less than optimal response.
VIII	1.82	7.95	3.08	10.38	17	Examen (1 c.c.)	Slightly less than optimal response.

Since Wills' work, crude liver extract was considered effective in the treatment of N.M.A. and purified liver extracts were presumed to lose the anti-anæmic principle which is supposed to be curative in the N.M.A. in the process of purification. Since then, however, it has been found that purified liver preparations are effective, but in larger dosage, than that for the P.A. The four cases quoted above show that purified liver extract Examen (New Potency) is also effective even in a small dose, 1 c.c., though it can be said that 3 c.c. produce better response than 1 or 2 c.c. Since the comparatively small dosage of refined liver extract used has produced optimum response, the cases in question seem to point the way to further investigations on similar lines.

The dosage of crude liver extract employed in the treatment of N.M.A. has been usually 2 to 4 c.c. daily (and even a bigger dosage for the first 2 or 3 days) for above 10 days, that is a total of 20 to 40 c.c. In the 4 cases of N.M.A. treated with crude liver extract the dosage was only 8 to 12 c.c. So far it has been the smallest dose found effective in our experiments.

Summary

1. The activity of three different types of liver extracts was investigated in cases of nutritional macrocytic anæmia.

2. It was found that pure liver extract (Examen, New Potency) gave optimum response in this anæmia; even small doses proved effective.

I take this opportunity of thanking the Dean, K. E. M. Hospital, and Honorary Director, Singhanee Hospital, for allowing me to report these cases. I also express my acknowledgment to the firms concerned for generously supplying me with liver extracts.

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STUDY OF LIVER DISEASES

CORRELATION OF CLINICAL AND LIVER FUNCTION STUDIES WITH LIVER BIOPSY

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IN cases of hepatic diseases it is at times difficult to arrive at a correct diagnosis from clinical findings only. To help the physician a number of laboratory tests have been devised. They include (i) the study of biopsy material, (ii) routine examination of blood and urine, and (iii) 'function tests' either to evaluate the impairment of the hepatic function or to study the derangement of some specific function of the liver. Such studies are necessary in cases where clinical signs like jaundice or ascites are present; and also in those where such signs are absent. It must be admitted that the liver 'function tests' have limited usefulness. The

possibility of impairment and the extent of derangement of the multiple functions of the liver are very large. No test is yet known which can be of a general diagnostic use. Till such test becomes available, which seems doubtful, the physician has to depend on the existent function tests of the liver, and choose therefrom those of value in particular cases. A second approach open to him will be to correlate the information available from the biopsy studies with the chemical tests.

We have been interested for some time in correlating the histology of the diseased liver with the tests of hepatic insufficiency. Studies of this type have been made by Hoffbauer, Evans and Watson (1945) in cases of cirrhosis of the liver.

In this paper, cases have been recorded where a definite histological diagnosis has been made from biopsy studies. In some, the necropsy material has also been employed.

Some of the 'function tests' performed are common both in the non-jaundiced and jaundiced cases. A few others have been taken up in jaundiced cases only. In non-jaundiced cases the tests performed were icteric index, quantitative serum bilirubin, quantitative urobilinogen, total and fractional serum proteins, hippuric acid synthesis, prothrombin time and response before and after administration of vitamin K, blood urea and non-protein nitrogen. In jaundiced cases, all these and faecal urobilinogen, serum cholesterol, van den Bergh's reaction and galactose tolerance test have been performed. The tests chosen were of general usefulness. The tests which are cumbersome to perform, have limited application and cause inconvenience to patients have been omitted. For our preliminary work cephalin-cholesterol flocculation test, bromosulphalein test and Takata-Ara test were performed. From them very little additional information was available, and as such they were abandoned at a later stage in our work.

The techniques employed are those commonly used in clinical laboratories. The estimations of total and fractional proteins have been made by the microkjeldahl method before and after precipitation with 22 per cent sodium sulphate. The blood urea has been determined by the urease-nesslerization method. The hippuric acid synthesis test has been performed by the intravenous method of Quick. The impairment of renal function, if any, was evaluated side by side by an injection of 1 c.c. of phenolphthalein and by determining the dye excretion after one hour; and also by the van Slyke's urea clearance test. For the determination of prothrombin time, one stage modified method of Quick has been employed. The prothrombin response was measured after an administration of 5 or 10 mg. of vitamin K parenterally. For urobilinogen the method of Wallace and Diamond has been employed.

Liver biopsy was performed with the Vim-Silverman needle. The technique has already been described in detail by one of us (Wahi, 1946).

Illustrative cases

Case I. Hindu female, aged 60 years, was admitted into the Thomason Hospital with the complaint of a painful lump in the right lumbar region of about two months' duration. There was a marked loss of weight, and signs of emaciation were present. The patient had jaundice, but there was no ascites or oedema. The liver was found enlarged, about four fingers below the costal margin, and was hard to feel. The pelvic examination revealed no abnormality. The patient's past history showed little of note. The working diagnosis of cancer of the liver was made.

The function tests performed in this case gave the following results: The stools were light yellow in colour and urobilinogen, as repeated examinations showed, was completely absent. Urine urobilinogen was 2 mg. The prothrombin concentration was 80 per cent, which, after an administration of 5 mg. of vitamin K, showed a rise to 88 per cent after 24 hours. The van den Bergh's reaction was immediate direct positive; serum bilirubin 3 mg.; icteric index was 35; blood cholesterol was 333.0 mg./100 c.c. and galactose 20 mg.; 0.25 gm. of hippuric acid was synthesized and the plasma proteins were found to be altered.

The function tests, by themselves, as can be seen from the data, could lead to no positive conclusion, some pointing towards hepatic lesions and others suggesting normal liver function. The photomicrograph of the needle biopsy (figure 1, plate XXV) shows no evidence of tumour. The canaliculi are dilated and contain bile thrombi. The liver cells show cloudy swelling. This suggests the diagnosis of extrahepatic biliary obstruction.

A detailed analysis of the case, therefore, shows that clinically the case labelled as cancer of the liver, when subjected to function tests, gave findings supporting the diagnosis either of cancer of the liver or extrahepatic biliary obstruction. The information obtained from the liver biopsy was of great value, and the case was labelled as one of extrahepatic obstruction.

Case II. T. S., Hindu male, aged 42 years, was admitted with a painful lump in the right hypochondrium of about three months' duration. He had jaundice four months before admission and had suffered from irregular fever during this period. A fortnight before admission he developed oedema of the feet. He had been a habitual alcoholic.

The examination revealed a poorly nourished, deeply jaundiced, slightly anæmic, middle-aged man. The liver was found to be irregularly enlarged from $\frac{1}{2}$ to 4 inches below the costal margin and was hard and slightly tender. Ascites was present and the spleen was not

palpable. After a few days' stay in the hospital there was a noticeable increase both in ascites and jaundice. The working diagnosis of cancer of the liver was made.

The prothrombin concentration was 70 per cent and was raised to 80 per cent after vitamin K administration; icteric index was 90; van den Bergh's reaction was immediate direct positive and serum bilirubin was 5.6 mg.; W.R. was negative and Takata-Ara test was positive; galactose was 40 mg. Blood urea was 35.6 mg; N.P.N. 32 mg.; total protein 4.8 per cent; serum albumin 2.9 grammes and globulin 1.9 grammes. The low plasma proteins and slightly altered A : G ratio indicated liver damage. Blood cholesterol was raised to 266.6 mg./100 c.c.; faecal urobilinogen was absent and hippuric acid synthesis was 0.42 gramme.

The liver function tests suggested the diagnosis of obstructive jaundice and liver damage and are quite in keeping with the clinical diagnosis of cancer of the liver.

The needle biopsy study of the liver (figure 2, plate XXV) revealed the presence of cancer and confirmed the diagnosis.

Case III. O. P., Hindu male, aged 23 years, was admitted with ascites of short duration. Five years back he suffered from fever with rigor which was controlled by quinine after a fortnight. He had also been getting epigastric pain.

The examination revealed a poorly nourished anæmic young man with no jaundice. He had ascites. The liver and the spleen were not palpable. The clinical diagnosis of endemic ascites was made.

Laboratory investigations showed: W.B.C. 5,000 per c.mm.; P—66; L—32; M—2; E.S.R. 14 mm.; van den Bergh's reaction was negative, icteric index 10 and serum bilirubin 0.35 mg.; prothrombin concentration of 66.6 per cent was raised to 80 per cent after administration of vitamin K. Takata-Ara test was positive. Blood urea was 34.2 mg.; N.P.N. 31 mg.; total proteins 5.87 grammes; serum albumin 3.55 grammes and globulin 2.32 grammes. Urine examination revealed the presence of urobilinogen and synthesis of 0.28 gramme of hippuric acid. Faecal urobilinogen was 100 mg. Examination of ascitic fluid showed cell count 37 per c.cm. which were all lymphocytes. Total proteins in ascitic fluid were 1.4 grammes.

Analysis of the findings does not lead one to any definite conclusion. The prothrombin concentration was low but showed a good response to vitamin K. Hippuric acid synthesis was very low and was the only finding which pointed towards liver damage.

The needle biopsy was done through the 10th intercostal route. The histological examination showed that the liver cells were markedly pigmented. The bile canaliculi were dilated and contained bile thrombi. The portal connective tissue was greatly increased and cellular. Newly formed bile ducts were present (figure 3,

plate XXV). Diagnosis: Cirrhosis of liver with jaundice.

The diagnosis of this case by needle biopsy was thus of great help as the case was believed to be one of endemic ascites. This also points to the fact that many of the so-called cases of endemic ascites if histologically examined may turn out to be those of cirrhosis of the liver.

Case IV. C., Hindu female, aged 45 years, was admitted into the Thomason Hospital with complaints of fever, cough with expectoration and constipation. There was history of previous attacks of malaria. The examination showed a fairly nourished woman with jaundice. The spleen was enlarged 5 inches and was hard and smooth. The liver was 5 inches below the costal margin, was hard and smooth. The working diagnosis of chronic malaria and cirrhosis of the liver with jaundice was made.

The laboratory investigations showed that the prothrombin concentration of 84.2 per cent was raised to 89 per cent after an administration of 10 mg. of vitamin K; icteric index was 17; van den Bergh's reaction indirect positive and serum bilirubin was 1.3 mg. Blood urea was 37.6 mg. and N.P.N. 34 mg./100 c.c. Total protein 5.2 per cent; serum albumin 3.8 per cent and serum globulin 1.4 per cent. Blood cholesterol was 160 mg./100 c.c. W.R. was negative and Takata-Ara test was positive. Galactose was 10 mg. Urine urobilinogen was absent and 0.39 gramme of hippuric acid was synthesized. Faecal urobilinogen was 150 mg.

The above findings show that most of the data are in favour of normal liver function except the low hippuric acid synthesis.

The liver biopsy (figure 4, plate XXV) revealed cloudy swelling, and no evidence of cirrhosis was present. Jaundice, probably of the hæmolytic type, was a result of malarial infection.

Case V. P. H., Hindu male, aged 40 years, was admitted for treatment. He gave a history of cough and expectoration, pain in abdomen and anorexia of about six months' duration. The patient had an attack of malaria four months back. He gave no history of amœbic dysentery.

He was markedly wasted and anæmic. There was no jaundice or ascites. The liver was found enlarged 1½ inches and was smooth, soft but not tender. The spleen was enlarged 5 inches below the costal region. It was hard and regular. Soft systolic murmurs were present in the pulmonary and mitral areas and crepitations were present in both lungs. The vocal resonance was diminished over the right base. The skiagram of the chest showed infiltration of the right lower and left middle zones. The working diagnosis of pulmonary tuberculosis was made. The cause for the enlargement of the spleen and the liver could not be definitely ascertained.

The laboratory findings in this case were R.B.C. 2,850,000 per c.mm.; hæmoglobin 7.5

grammes; W.B.C. 4,600 per c.mm.; P—76; L—21; M—2; E—1; M.C.V. 100 cu μ ; M.C.H. 26 μ v; M.C.H.C. 26 per cent; reticulocytes 1 per cent; prothrombin concentration was 61 per cent and was raised to 76 per cent after an administration of 10 mg. of vitamin K. Icteric index 6; van den Bergh's reaction was negative and serum bilirubin was less than 0.25 mg. Blood urea was 39.8 mg.; N.P.N. 36 mg./100 c.c.; total protein 4.7 per cent; serum albumin 2.8 per cent and serum globulin 1.9 per cent; W.R. was negative. Urine urobilinogen was 10 mg. Faecal urobilinogen was normal. Hippuric acid synthesis was 0.9 gramme. The sputum on repeated examination was negative for acid-fast bacilli. The analysis of the function tests showed a low prothrombin response after vitamin K injection pointing towards liver damage.

The needle biopsy of the liver was performed and showed the presence of amyloid disease (figure 5, plate XXV), a finding which was rather unexpected in view of the absence of any chronic suppurative lesion or evidence of neoplasm. The x-ray examination had shown pulmonary tuberculous infiltration but there was no evidence of caseation or cavity formation.

The case was one of amyloid disease of the liver following pulmonary tuberculosis.

Case VI. D. H. M., aged 15 years, was admitted into the Thomason Hospital with complaint of enlarged spleen and liver. He suffered from malaria for six months about two years back. The spleen was enlarged since then while the liver has been enlarged for the last six months.

He was a young boy of good build, slightly anæmic. There was no jaundice or ascites. The spleen was hard and smooth, 8 inches below the costal margin. The liver was felt 3 inches below the costal margin. It was smooth, moderately hard and not tender. The working diagnosis of chronic malaria and cirrhosis of the liver was made. Kala-azar was also thought to be a possibility and so also megalocytic anæmia.

The laboratory investigations showed: R.B.C. 2,150,000 per c.mm.; Hb. 5.5 grammes; W.B.C. 4,400 per c.mm.; P—55; L—42; M—3; P.C.V. 21 per cent; M.C.V. 100 cu μ ; M.C.H. 26 μ v; M.C.H.C. 26 per cent. The prothrombin concentration of 84 per cent was raised to 100 per cent after vitamin K. Icteric index was 8 and serum bilirubin was 0.3 gramme. Blood urea was 28.5 mg.; N.P.N. 25.6 mg.; total proteins 5.6 grammes; serum albumin 3.2 grammes and globulin 2.4 grammes. Aldehyde and antimony tests for kala-azar were negative. Hippuric acid synthesis was 0.9 gramme. Urine showed excess of urobilin.

From these findings the liver could be assessed as perfectly normal, the cause for the enlargement remaining undetected. The needle biopsy of the liver showed increased cells in the

sinusoids and portal tracts. The cells gave the impression of being formed from sinusoidal epithelium. The picture (figure 6, plate XXV) suggested histiocytic medullary reticulosis. No changes suggesting cirrhosis were present.

The case illustrates that the part liver biopsy may play in the detection of the cause of liver enlargement where the function tests are perfectly normal.

Case VII. S., Hindu female, aged 38 years, was admitted with a history of fever for seven months, pain in abdomen and indigestion. She had been having attacks of dysentery for the last 1½ years. There was an attack of malaria about an year back lasting for about two months.

She was a poorly nourished and anæmic woman. There was no jaundice but there was slight ascites. She had a low temperature ranging between 99° and 100°. Oedema was present in both the legs. The liver was enlarged 6 inches below the costal margin. It was smooth, hard and slightly tender. The spleen was not palpable. Working diagnosis of amoebic hepatitis was made.

Laboratory investigations showed: R.B.C. 2,000,000 per c.mm.; Hb. 4 grammes; W.B.C. 6,150 per c.mm.; P—86; L—13; M—1; P.C.V. 15 per cent; M.C.V. 75 cu μ ; M.C.H. 80 μ v; M.C.H. 26 per cent; prothrombin concentration was 100 per cent; icteric index 18; serum bilirubin 0.4 mg.; blood urea 36.4 mg.; N.P.N. 33 mg.; total proteins 5.24 grammes; serum albumin 2.8 per cent; serum globulin 2.44 per cent; blood cholesterol was 230 mg. per 100 c.cm.; W.R. negative. Urine urobilinogen was 10 mg. and 0.38 gramme of hippuric acid was synthesized. Faecal urobilinogen was 200 mg. The sputum showed pus cells and the usual oral flora.

The analysis of the findings show that liver damage was indicated by the low hippuric acid synthesis and jaundice. The patient was given 12 emetine hydrochloride injections of 1 grain each with no improvement.

The liver biopsy was done (figure 7, plate XXVI) and the histological examination showed portal cirrhosis. In spite of the cirrhotic condition, the liver-prothrombin concentration was normal. Though damaged liver was diagnosed the cause of it was only located after biopsy.

Case VIII. L., Hindu male, aged 45 years, was admitted with the complaints of fever for 4 months, swelling of feet, scanty urine and ascites, all of about 3 months' duration. The examination revealed that the patient was anæmic and had ascites. The spleen was enlarged 3½ inches and the liver was not palpable. After paracentesis abdominis, the liver was still not felt.

The working diagnosis of ascites secondary to atrophic cirrhosis of the liver was made.

The laboratory investigations revealed prothrombin concentration of 53.3 per cent raised to 64 per cent after vitamin K. Icteric index 3; serum bilirubin normal. Blood urea 47.6 mg.;

N.P.N. 42.8 mg.; total protein 4.9 grammes; serum albumin 2.5 grammes; serum globulin 2.4 grammes and hippuric acid synthesis of 0.5 gramme. Urine urobilinogen was normal. Faecal urobilinogen was present. The protein of the ascitic fluid was 3.8 per cent.

The liver biopsy by needle did not enable us to secure specimen for the histological examination. Later, after the patient died, post mortem was performed. The histological examination of the liver tissue (figure 8, plate XXVI) showed miliary tuberculosis of the liver and the capsule. Low prothrombin response and low hippuric acid synthesis suggest a damaged liver but the cause of the damage presumed to be cirrhosis of the liver was due to tuberculosis of the liver. Ascites was due to tuberculous peritonitis.

Conclusions

1. A few cases of hepatic diseases have been presented in which from clinical findings alone difficulty was experienced in making a correct diagnosis.

2. Liver biopsies have been carried out with the Vim-Silverman needle, and the histological picture of each has been presented as micro-photographs.

3. A number of function tests have been performed in each case and the findings have been presented.

4. An attempt has been made to correlate the clinical, chemical and histological findings, and difficulties in the interpretation of function tests have been pointed out.

5. Single tests have been found useless in the assessment of the nature and extent of hepatic impairment. It has been found that a combined study of the liver functions and the histological findings gives a better information about the nature and extent of the liver diseases. The cause of liver damage in most cases can be definitely established by biopsy studies alone and from the characteristic profiles it is hoped that the extent of hepatic impairment can be properly assessed.

6. Comparative value of the various liver function tests has been assessed, as the correct diagnosis of the nature of the liver affection was possible by the histological examination of the biopsy material.

Our thanks are due to Major-General H. C. Buckley, I.M.S., Superintendent, Thomason Hospital, and Principal, Medical College, Agra, for the facilities given to us for carrying on this work; to Drs. G. N. Vyas, K. N. Gaur and B. K. Dube, physicians, for allowing us to perform the liver biopsy and function tests on their cases; and to Drs. Kashi Nath and V. N. Tiwari, for assisting us in the work.

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BASAL METABOLIC STUDIES IN THE PUNJAB

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It had long been felt that while valuable work on basal metabolism had been done in Bengal (Bose and De, 1934; Mukherjee and Gupta, 1931), Madras (Krishnan and Vareed, 1932; Mason and Benedict, 1931), Bombay (Sokhey and Malandkar, 1939; Niyogi, Patwardhan and Mordecai, 1939; Niyogi, Patwardhan and Sirsat, 1941), Lucknow (Banerji, 1931), Hyderabad, Deccan (Rahman, 1936) and Coonoor (Rajagopal, 1938) no normal standards were available for the Punjab which differs from other provinces of India chiefly in having wheat-eating population, better physique and extremes of climate. There is considerable evidence that dietetic, climatic and occupational factors influence basal metabolism. Basal metabolic rate in other provinces of India deviates markedly from the accepted American and European standards. This observation made the demand for an investigation of the standards in the Punjab all the more important.

Though this work was undertaken with this limited objective yet the greatest possible accuracy in the experimental technique was aimed at and full data were recorded with a view to make this study serve a somewhat wider purpose. The investigation is limited to one hundred individuals only, comprising sixty males and forty females, mostly medical students and members of the college staff, between the ages of 16 and 36 years, representing all communities.

Experimental

The usual standard precautions, namely 14 to 16 hours' fasting, least muscular exertion, mental repose, etc., were strictly adhered to in the preparation of the cases who were otherwise quite fit and healthy. The investigation was carried

out by the Douglas' bag and Haldane's general air analysis apparatus.

B.M.R. was calculated in terms of heat production per 1 square metre of body surface per 1 hour from the respiratory quotient and surface area. In the first ten cases two observations on each case were made on two consecutive days but in all these the difference was negligible. The duplicate observations were thus omitted in the rest of the cases.

Results.—The average basal metabolic rate was 35.66 ± 3.81 and 35.11 ± 3.4 with a range from 29.0 to 41.3 and 30.1 to 40.7 calories per 1 hour per square metre for sixty males and forty females respectively.

Due to want of space the results of all the hundred cases are not given. They are

represented, however, in a condensed form in table I.

Out of one hundred cases given in table I 30 were strict vegetarians (excluding even eggs). It was observed that B.M.R. was 32.9 calories in vegetarians against 35.8 calories in non-vegetarians.

Regarding age, majority of the subjects were adults between the ages of 16 and 36 years. Charts I and II indicate that basal metabolic rates decrease with increase of age.

The results on the whole are lower than the accepted American and European standards by —10.5, —13.2 and —13.4 in males and —9.5, —10.6 and —5.7 in females from Harris Benedict, Aub Dubois and Boothby Sandiford standards respectively.

TABLE I

Basal metabolic rate in normal individuals

Number of cases	Range of B.M.R.	Average B.M.R. (1 hr. 1 sq. m.) calories	Percentage deviation from		
			Harris Benedict	Aub Dubois	Boothby Sandiford
60 males					
4	Under 30	29.3	- 21.35	- 26.7	- 27.6
7	30-33	31.6	- 17.8	- 21.6	- 22.4
23	33-36	34.6	- 10.2	- 14.3	- 14.7
13	36-39	36.9	- 5.4	- 9.2	- 9.5
13	Above 39	40.3	+ 2.8	- 2.2	- 2.5
Average of 60 cases	35.6	- 10.5	- 13.2	- 13.4
40 females					
Nil	Under 30	..			
11	30-33	31.2	- 16.7	- 16.3	- 13.9
14	33-36	34.5	- 10.2	- 10.7	- 5.7
7	36-39	36.7	- 3.7	- 1.6	+ 0.6
8	Above 39	39.9	+ 4.4	+ 1.6	+ 8.2
Average of 40 cases	35.1	- 9.5	- 10.6	- 5.7

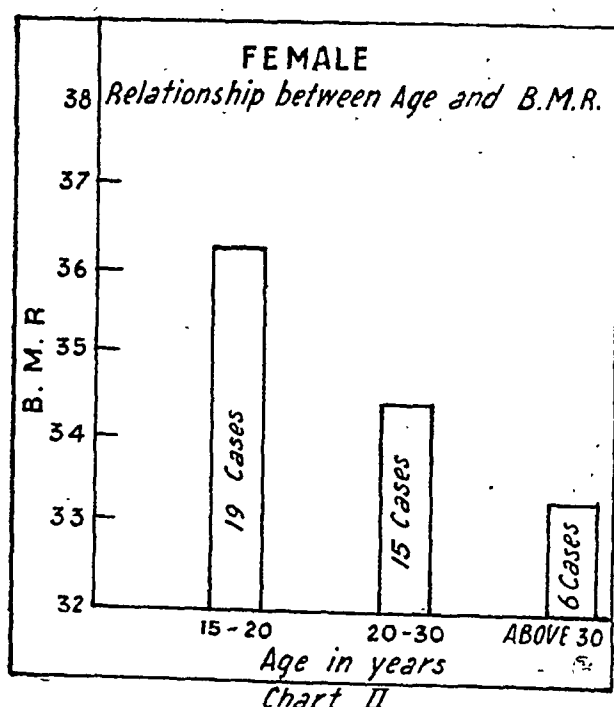
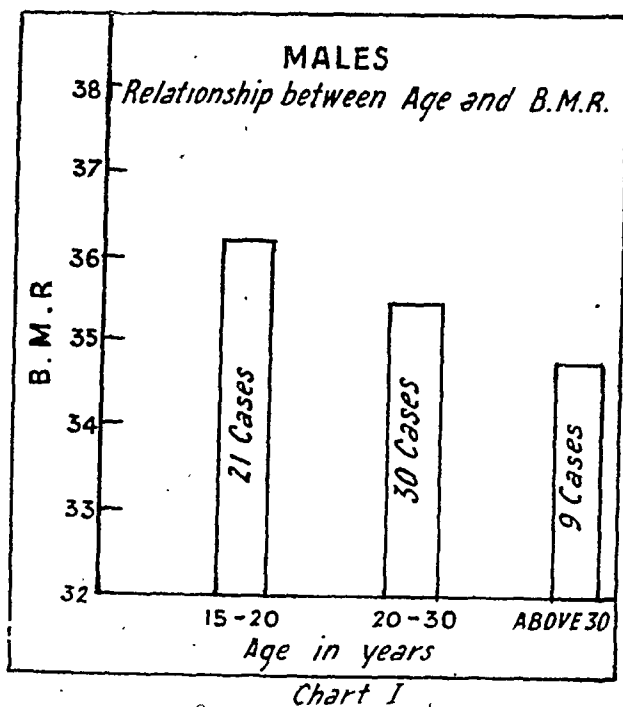


TABLE II
Results of physical examination of 100 cases

Physical examination	AVERAGE WITH MEAN DEVIATION		RANGE	
	Males	Females	Males	Females
Pulse rate (1 min.) ..	72.08 \pm 8.2	75.57 \pm 7.5	55-92	52-90
Respiratory rate (1 min.) ..	15.4 \pm 2.4	17.37 \pm 3.3	12-30	14-24
Systolic blood pressure (mm. Hg.) ..	104.4 \pm 11.2	108.6 \pm 9.5	90-132	94-130
Diastolic blood pressure (mm. Hg.) ..	75.6 \pm 5.5	76.4 \pm 6.8	64-68	60-90
Pelidisi ..	95.03	99.25	88.4-107.3	88.2-114.9
Vital capacity (c.c.) ..	3,669.1	2,430.6	2,300-5,000	1,700-3,500

Note.—Pelidisi (Pirquet, 1922) = $3 \sqrt{10 \times \text{wgm.}} \div \text{sitting height (in cm.)} \times 100$.

In addition physical examinations given in table II were conducted in each case.

Attempts were made to correlate these with B.M.R. but there seems to exist no correlation between them. Details of the statistical data are not given here due to want of space.

It was, however, observed that B.M.R. during menstrual period was below the average. The post-menstrual group showed higher B.M.R. than the pre-menstrual one.

In table III are given the various ranges of B.M.R. in each menstrual cycle.

TABLE III
B.M.R. in menstrual cycle

Menstrual cycle	Number of cases	Average B.M.R. (calories 1 hr. 1 sq. m.)	Range
Actual menstruation.	2	32.5	30.9-34.1
Pre-menstrual ..	10	34.89	30.8-40.0
Post-menstrual ..	10	36.9	30.8-40.6
Interval ..	7	34.4	30.9-40.7

Summary

1. An investigation of basal metabolic rates on 60 normal adult males and 40 females mostly Punjabi students between the ages of 16 and 36 years has been carried out by the Haldane's general gas analysis apparatus.

2. Like that of other Indian workers our average B.M.R. is low both in males and females as compared with American and European standards. The females do not show results particularly lower than the males. It is just possible that this low B.M.R. of Indians may be due to difference in diet. Further work is needed to elucidate the point.

Acknowledgment

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MYOEPIHELIAL TUMOURS OF THE SALIVARY GLANDS *

REPORT OF THREE CASES

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THE histogenesis of the mixed salivary tumour is still a debatable question. The cytological appearances are of a varied nature and it is because of this baffling histology that these neoplasms have been variously called as enchondromas, endotheliomas and basal cell carcinomas.

During the last 5 years 50 salivary gland tumours were studied in this laboratory. The material was classified as follows:—

Salivary gland tumours:	Total ..	50
Carcinoma	15
Mixed salivary gland tumours	27
Cylindroma	4
Onkocytoma	4

* A study under Dr. V. R. Khanolkar, b.sc., M.D. (Lond.), Director of Laboratories.

The distribution of the 27 mixed salivary gland tumours was as follows:—

Parotid 20
Submaxillary 4
Palate 3

All the salivary glands have a common plan of origin and development. The primordium arises as an epithelial bud and grows by branching into solid ducts whose ends round out into secretory acini. Secondary hollowing of the whole system and specialization of the acinal cells complete the epithelial differentiation.

The principal feature of the salivary gland is the epithelial cell which is cuboidal in shape. These cells produce either mucus or serous secretion and are arranged round a clearly defined lumen. A second type of cell is seen between the secreting epithelium and the basement membrane. These are either stellate cells or elongated spindle-shaped cells. They have been called the basket cells. It is generally accepted that these cells are ectodermal in origin and it has been suggested that they possess contractible properties.

Both these types of cells are normally present in the salivary glands, the one represented by the secreting epithelium and the other by the basket cell. It has recently been suggested by Sheldon (1941) that the majority of neoplasms of salivary gland arise from epithelium, and that an excessive or an abnormal secretion from the tumour cells produces a myxomatous change or even a pseudocartilaginous alteration in the connective tissue stroma. True cartilage may be present and is formed by metaplasia of the stromal tissue. These common tumours usually known as mixed tumours of the salivary glands belong to group I of Sheldon's classification. Other neoplasms arise from both the epithelium and the basket cells. These are truly organoid tumours (Sheldon, gr. II). It has been suggested that in some rare tumours the basket cells alone take part in the neoplastic proliferation. Such tumours bear great resemblance to myoepithelial tumours and may be designated group III (Sheldon).

On the basis of these suggestions the 27 mixed salivary gland tumours studied in this department could be classified as follows:—

	Group I	Group II	Group III
T. M. H. Non-cancerous	16	8	3
Cancerous ..	1	..	1
Sheldon Non-cancerous	19	20	2
Cancerous	5	1

Three case reports of myoepithelial tumours are presented below. The myoepithelial cells should be considered epithelial in nature but by shape and structure are indistinguishable from smooth muscle cells. Kolliker stated that myoepithelium has the faculty of very readily

changing into cuboidal morphology. This is seen in one of the microphotographs presented (figure 2, plate XXVI).

Case 1 (D 1140)

A male patient complained of a swelling in the region of the parotid gland of 4 years' duration. The swelling to start with was of the size of an apricot seed and was freely movable.

Gross observations (figure 1, plate XXVI).—Smooth hemispherical piece of tissue, whitish opaque in colour and measuring 2 cm. in diameter. The cut surface shows a central cystic cavity roughly 1 cm. in diameter. Small papillary projections are seen arising from the wall into the lumen of the cyst.

Microscopical observations.—Under the microscope are seen fusiform cells which resemble the basket cells of the salivary gland acini (figure 2, plate XXVI). The neoplastic cells are arranged in closely packed interlacing bundles. The nuclei are ovoid in shape with uniformly scattered chromatin material. The stroma is fairly well vascularized and shows abundant hyaline material. The tumour cells do not show the morphological characters usually associated with malignant proliferation.

Case 2 (D 1272)

A male patient, aged 18 (figure 3, plate XXVI), was admitted to the hospital on 1st November, 1944, with a swelling in the region of the left parotid gland of 1 year's duration. The patient noticed a painless, roundish swelling about the size of a betel-nut in the lower part of the left side of the neck. The swelling gradually increased in size. On examination it was found that there was a firm and roundish swelling fixed to the deeper structures. The tumour was removed by operation.

Gross observations (figure 4, plate XXVII).—The specimen measured 8 × 5 × 4 cm. It presented on cut section dense greyish appearance with scattered yellowish areas. A portion of the tumour showed brownish area of hæmorrhage.

Microscopical observations (figure 5, plate XXVII).—The section through the tumour shows interlacing bundles of fusiform cells. The nuclei of the tumour cells are ovoid in shape and contain densely scattered chromatin material. Each nucleus contains a single prominent nucleolus. The nuclei are mostly of uniform size and shape but at places are seen hyperchromatic nuclei with frequent mitosis. The 'Gomori' method of staining shows reticulum passing round groups of tumour cells (figure 6, plate XXVII).

Case 3 (E 1392)

A male patient, aged 40, noticed a painless lump on the right side of the upper portion of his neck about 1 year ago. It is tender for the last 6 months. On examination there is seen a firm, nodular, smooth, slightly tender lump occupying the right side of the upper portion of

the neck and angle of the right mandible pushing the lobule of the right ear upwards. It is fixed to the deeper structure and adherent to the skin.

Gross observations.—A specimen of the tumour $5 \times 3\frac{1}{2} \times 2$ cm. It is firm to feel, nodular on surface and shows on cut section scattered areas of necrosis. The greyish tumour mass seems to be made up of fusiform bundles which are rather dense and homogeneous in appearance. Interspersed is brownish homogeneous looking tissue.

Microscopical observations (figure 7, plate XXVII).—Show bundles of fusiform cells separated by areas of necrosis and hæmorrhage. The cytoplasm of the tumour cells is basophilic. The nuclei are ovoid in shape with uniformly scattered chromatin material. They are of uniform size. The cytology of the tumour cells do not suggest a malignant change.

Comment

The question of histogenesis of the mixed salivary gland tumour does not seem to have been settled. The classification suggested by Sheldon seems to be a more plausible one. On the basis of this classification it has been possible to grade the neoplasms studied in this laboratory. Figure 1 shows that the myoepithelium can have cuboid morphology. Figure 2 shows a malignant transformation in a myoepithelial tumour.

Summary

1. A brief review of the histogenesis of mixed salivary tumour is presented.
2. Mention is made of Sheldon's classification of salivary gland tumours with a special stress on the myoepithelial variety of tumours.
3. Three cases of myoepithelial tumours are reported, one of these showing evidence of malignancy.

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Description of plates XXVI and XXVII

Figure 1. Case 1 (D 1140): Cut surface of the specimen showing a central cystic cavity.

Figure 2. Case 1 (D 1140): Microphotograph shows that the myoepithelium can have cuboidal morphology.

Figure 3. Case 2 (D 1272): Photograph of a patient with a swelling in the region of left parotid gland. The swelling first noticed in the lower part of the left side of the neck.

Figure 4. Case 2 (D 1272): Cut surface of the specimen showing dense appearance. Scattered areas of hæmorrhage are also seen.

Figure 5. Case 2 (D 1272): Microphotograph shows interlacing bundles of cells. Hyperchromatic nuclei and mitotic figures are seen at places.

Figure 6. Case 2 (D 1272). The 'Gomori' method of staining shows reticulum passing round groups of tumour cells.

Figure 7. Case 3 (E 1392): Microphotograph shows bundles of fusiform cells separated by areas of necrosis. The nuclei are of uniform size and shape. Cytology does not suggest a malignant change. Compare microphotograph of case 2, figure 5.

ACHALASIA CARDIA (CARDIOSPASM)

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CARDIOSPASM is a functional type of obstruction of the œsophagus. It passes through the diaphragm into the lower part of the thoracic œsophagus. This was first described by Hanney in 1833. In 1882 Mikulicz suggested that it was due to the spasm of the cardiac sphincter. In 1915, Hurst introduced the word achalasia cardia, meaning absence of relaxation of the cardiac sphincter.

Pathology

It was believed by the earlier writers that the condition was due to diminished contractile power or general weakness. This view fails to explain hypertrophy which is always present and which indicates that the œsophagus must have made violent efforts to overcome some obstruction. The cardiac sphincter in these cases does not offer resistance to a weighted bougie or the examining finger at the autopsy. This led Rolleston in 1895 to suggest that the dilatation of the œsophagus might be due to a failure in the co-ordinating mechanism by which the cardiac sphincter is relaxed during swallowing. He suggested paralysis or continued inhibition of the longitudinal muscle fibres of the œsophagus would allow dilatation of the tubes to occur and at the same time by interfering with the opening of the cardiac sphincter would induce hypertrophy of the circular muscular coat. Hurst believes the condition to be a neuromuscular imbalance (Auerbach's plexus). In cardiospasm there is a failure of the abdominal œsophagus to relax in front of the wave of contraction which is carrying the bolus of food through the œsophagus.

Symptoms

A good history gives away the diagnosis. Usually the symptoms start after some nervous strain and has been known to occur under conditions of stress and strain. A number of cases

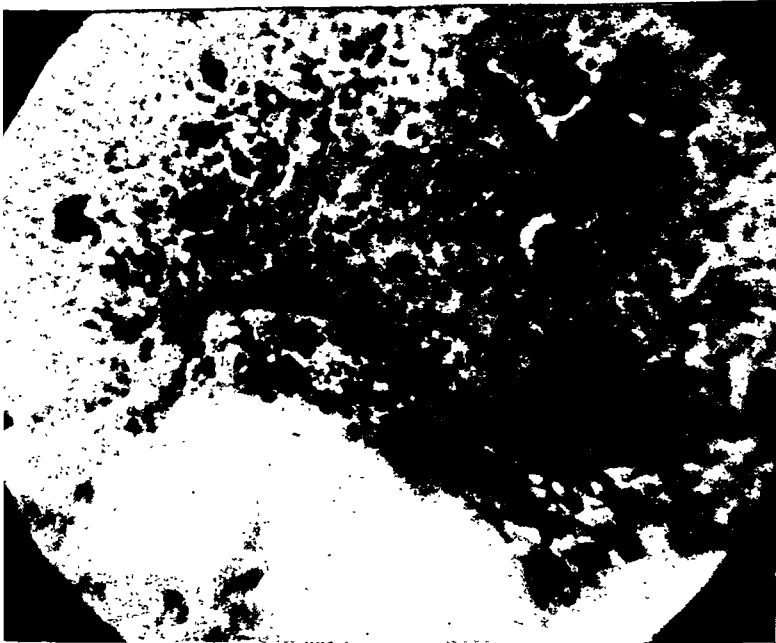


Fig. 1.—Case I.

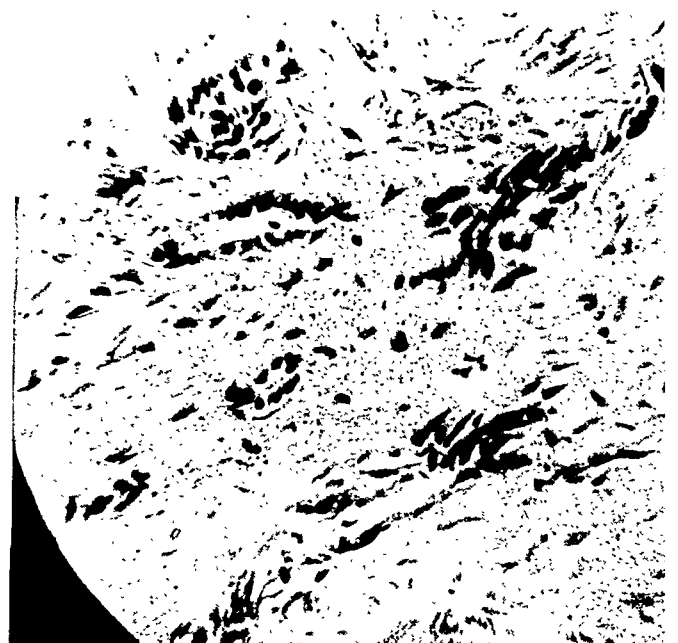


Fig. 2.—Case II.

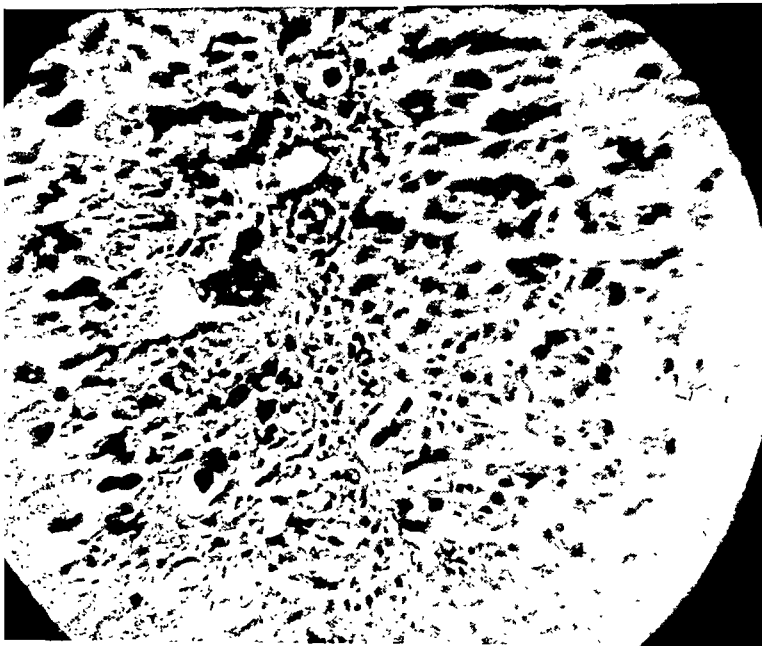


Fig. 3.—Case III.

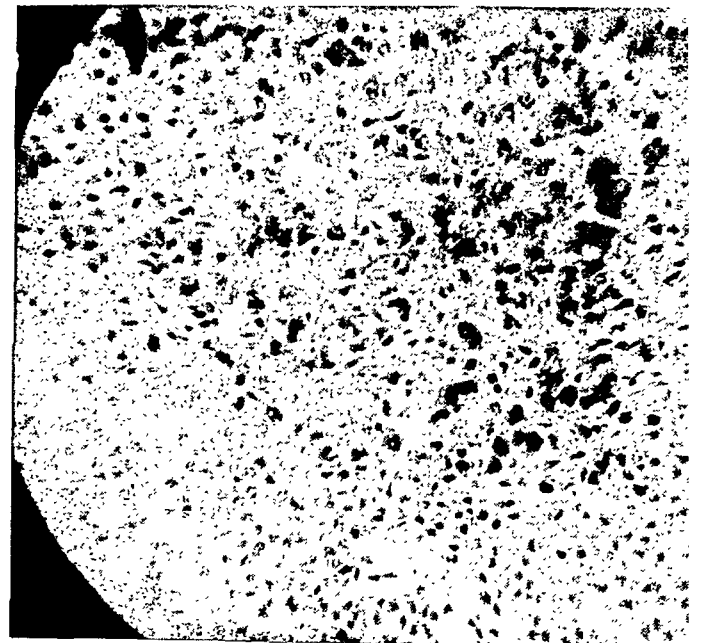


Fig. 4.—Case IV.

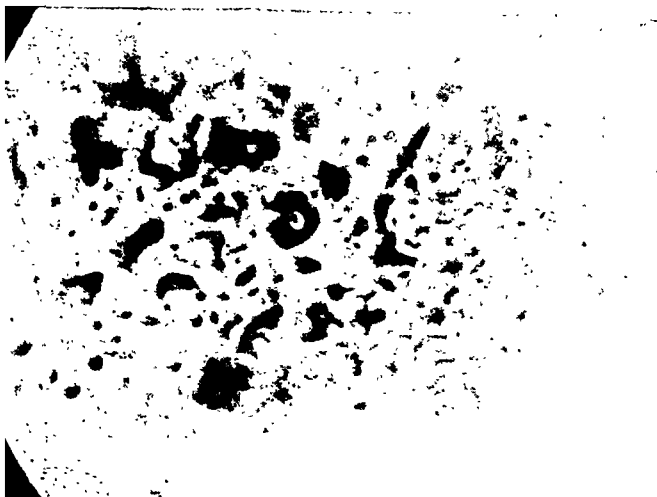


Fig. 5.—Case V.

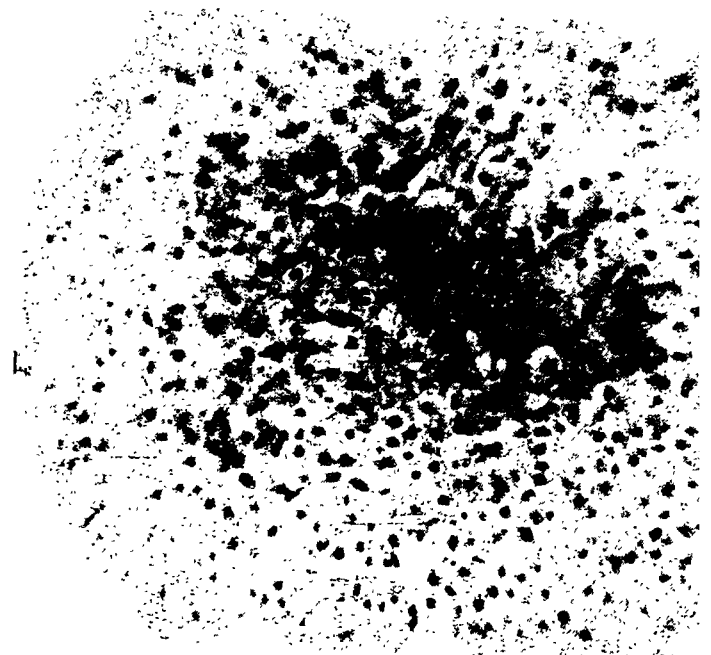


Fig. 6.—Case VI.



Fig. 1.—Esophagus filled to a height of nearly 6 inches and fundus of the stomach showing air.



Fig. 2.—Megacolon.



Fig. 3.—Mega-pelvis and mega-ureter.

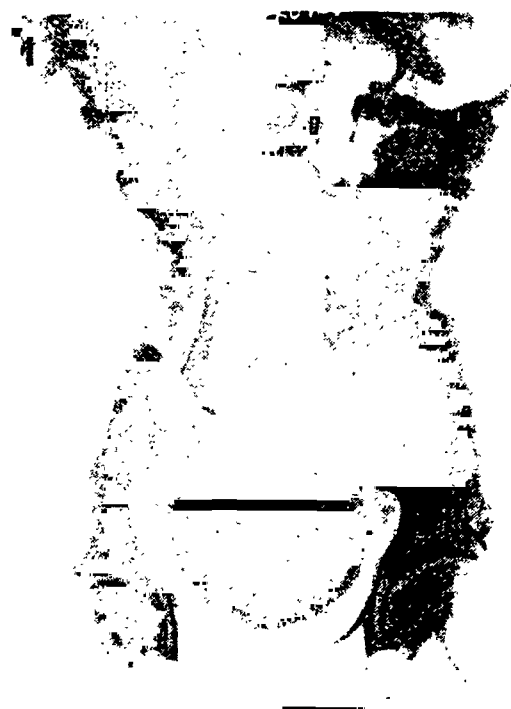


Fig. 4.—Dilated ureters and pelvis including bladder.

have been observed by Hurst in men on active military duty. The complaints are often slight pain or discomfort of a sensation of pressure or burning in the oesophagus or under the sternum. The patient says that he has a feeling of the food being held up at the level of the xiphisternum and as he goes on taking more and more food he feels the sensation of the food entering into the stomach. He feels the oesophagus is not empty. Sometimes discomfort is referred to the neck, lower jaw, or the region of the ears. Sometimes the pain may simulate angina pectoris. Wolferth and Edeiker state that 'any patient who is supposed to have attacks of angina pectoris which come on spontaneously or as a result of mental perturbation, which cannot be provoked by exertion or be relieved by nitro-glycerine, we class as an oesophageal spasm suspect until proved to the contrary'. These patients may be free from the symptoms for some time without any treatment whatsoever and then the symptoms may recur. X-ray studies with barium swallow clinch the diagnosis. Barium fills the oesophagus and gives it the appearance of a stomach in the thorax. The end of the oesophagus is smooth and regular and the barium stands to a height of 6 inches. In long-standing cases the oesophagus may be dilated to such an extent as to cause a twist and produce a 'S'-shaped organ.

Treatment

The treatment in the earlier cases is to dilate by mercury bougies and then to feed the patient. The patient is trained to pass the bougies himself. Once he is capable of passing it himself he continues it for some time till the food passes normally. Then the bougies are passed only once in a way when the patient feels there is a tendency for the symptom to recur. Where the bougies do not give a satisfactory result surgical treatment is indicated. The common procedure is to do a gastrostomy and dilate the cardiac sphincter from below. Other methods advocated are psychotherapy, sedatives and antispasmodics. In my cases the usual sedatives and antispasmodics did not give any appreciable result. Mercury bougies give the most satisfactory results. I am reporting the following case because the patient had, in addition to achalasia, mega-ureters and mega-colon. In 1944, Hurst reported in achalasia cardia that air in the fundus of the stomach was not present but in the case that I am reporting it was present as is shown by the x-ray film.

Case report

Kondiah : Hindu male, aged 15 years, admitted for dysphagia of three years' duration; history of dysentery three years ago. No other member of the family (five brothers and four sisters) affected.

The patient had severe burning pain in the chest for some days after an attack of dysentery three years ago. Subsequently he had dysphagia.

The present complaint was that he was not able to swallow freely. Had a feeling that the first mouthful of food was held behind the upper part of the body of the sternum and on taking some more mouthfuls it passed on. The same effect occurred on taking a glass of water.

Barium swallow and screening.—Achalasia cardia was present. Barium was held up to the level of the clavicle. There was air in the fundus of the stomach (figure 1, plate XXVIII); general condition good. Mercury passed easily and after the passage of the bougie, the patient swallowed a tumbler of water freely. He was put on sedatives and belladonna without any relief. As he did not get good relief if the bougies were not passed before taking food every time, gastrostomy was done and cardiac sphincter was dilated through the stomach. Because of the incidence of the disease at a very young age barium meal series was done and it showed marked dilatation of the rectum and sigmoid colon (figure 2, plate XXVIII) and a pyelogram picture showed hydro-ureters with spasm of the ureteral junction with the bladder (figures 3 and 4, plate XXVIII).

My thanks are due to the Superintendent, Government General Hospital, for permission to report this case, to Dr. T. Satagopan, M.B., under whose care the patient was admitted and to Dr. B. M. Sundaravadaman, who did the operation on the patient, and the pyelogram series.

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AMOEBIC GRANULOMA (AMCEBOMA) OF THE LARGE INTESTINE

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SURGICAL complications in intestinal amoebiasis are not unknown, but the comparative rarity of case reports in India and the diversity of clinical pictures render it necessary to record the six cases we have come across from the year 1940. Hummel (1940) has pointed out that amoebic granuloma of the large intestine while not common has been reported sufficiently often for the surgeon to be on his guard when making a diagnosis of new growth. Vaccarezza and Finochietto (1920), James and Deeks (1924), Gunn and Howard (1931) and De Paula and Frota (1941) mention occlusion and sub-occlusion amongst the surgical complications in this condition. Ochsner and De Bakey (1942)

in a collective review, considering all the complications *in seriatim*, described in detail the amœbic granuloma and by virtue of its resemblance to a new growth in appearance and effects called it the 'amœboma'.

The six cases under review were all admitted into the General Hospital, Madras, with signs of intestinal obstruction. In three, the fæces were not examined because the nature of the condition was not suspected, while amœbæ were seen in two of the other three cases.

Case 1.—S., a Hindu male, aged 34, was admitted on 11th September, 1940, with a complaint of pain in the abdomen coming on at irregular intervals and passing blood and mucus with very little fæcal matter. A freely movable lump was felt in the umbilical region. Skiagrams taken after barium enema showed filling defect in the cæcum. A provisional diagnosis of chronic intestinal obstruction was made, and an irreducible large-sized ileocæcal intussusception mass noticed on opening the abdomen was resected. No record of the follow-up of the case is available since the patient was discharged from the hospital against medical advice.

Specimen: Macroscopic appearances—The sausage-shaped intussusception mass measured about 5 inches in length. On opening the ensheathing layer, the intussusceptum was found gangrenous covered with shreds of necrotic mucous membrane (figure 1, plate XXIX). Microscopically, the mucosa and sub-mucosa showed varying degrees of necrosis with congestion and œdema of the deeper layers (figure 2, plate XXIX). Though the cellular reaction was mainly mononuclear many polynuclears were found probably due to infection with secondary organisms. In the muscular layer, clusters of amœbæ were seen (figures 3 and 4, plate XXIX).

Case 2.—R., a well-nourished Hindu male of 25 years, was admitted on 29th January, 1942, for continuous pain of two weeks' duration in the right iliac fossa, bearing no relation to food. His abdomen moved freely with respiration, but the right rectus was rigid. A tender mass, 4 inches by 1½ inches, was palpable in the right iliac fossa not adherent to the anterior or posterior abdominal wall. During operation, an intussusception was found in the region of the cæcum which on reduction showed a tumour. The mesenteric lymph nodes were enlarged. The terminal portion of the ileum, cæcum, ascending colon and the right half of the transverse colon were resected. Smears made from the ulcerated, necrotic, oval tumour mass in the cæcum revealed active *E. histolytica*. Nine grains of emetine were given after operation and the patient was discharged cured on 13th February, 1942, passing semi-solid motions.

Specimen: Macroscopic appearances—The cæcum just above the ileocæcal junction showed a raised circular mass 2.5 inches in diameter with marked peripheral necrosis and central intact mucosa (figure 5, plate XXIX). A small

typical amœbic ulcer was seen in the hepatic flexure but the rest of the mucosa was almost normal.

Microscopic appearances—The superficial layer consisted of degenerated cells. Beneath the necrotic zone, in the deeper layers of sub-mucosa, congested vessels with hæmorrhages, swollen connective tissue fibres separated by œdema fluid, monocytes and large collections of polynuclears were discernible. The inflammatory changes extended into the muscular and the serous coats. Amœbæ were found scattered in all coats.

Case 3.—V., a Hindu male of 25 years, was admitted on 10th May, 1943, with a history of assault three days prior to admission and a painful lump in the umbilical region, passing mucus and blood per rectum since the previous day. There was no history of vomit, nor was there tenderness or rigidity over the lump. Barium enema showed filling defect of the cæcum. In the motion were seen R.B.C.s and mucus but no amœbæ. During operation on 12th May, 1943, an irreducible ileocæcal intussusception was noticed. The last foot of the ileum, ascending and right third of the transverse colon were resected and a side-to-side anastomosis done. Recovery was uneventful and the patient was discharged cured after a full course of emetine injections.

Specimen: Macroscopic appearances—Due to adhesions, the intussusceptum could not be separated from the intussusciens. On opening the gut the mucous membrane covering the intussusceptum was found gangrenous with a nodular mass of about 1½ inches size at the tip of the intussusceptum (figure 6, plate XXIX). In addition, isolated ulcers were present in the ascending colon. The microscopic appearances were the same as in the two previous cases, showing amœbæ.

Case 4.—V., a male, aged 40, was admitted on 1st June, 1944, with a complaint of colicky abdominal pain and melæna since five days. He was ill nourished, anæmic and unable to retain feeds. An oval firm tumour mass, moving with respiration, not fixed to the anterior or posterior abdominal mass, was palpable in the right lumbar and umbilical regions. The right iliac fossa felt empty in contrast to the left. On 3rd June, 1944, for screening and roentgenography a barium enema was administered which reduced the intussusception. Another attack on 4th June, 1944, necessitated an operation which revealed a reducible cæco-colic intussusception below the under-surface of the liver, its apex being formed by an indurated depressed ulcer. A hemicolectomy with side-to-side anastomosis was done. The motion showed R.B.C.s, epithelial and pus cells and *E. histolytica*. The patient expired two days after the operation. No emetine was given.

Specimen: Macroscopic appearances—A hemispherical mass, half the size of a tennis ball,

was found in the cæcum just beyond the ileo-cæcal junction. The summit of the mass was gangrenous, surrounded by ulcerated oedematous folds of mucous membrane (figure 7, plate XXIX). A number of small undermined ulcers were seen in the mucous membrane of the ascending colon. Microscopic appearances were similar to those described already. Numerous amœbæ were found in the submucous layer.

Case 5.—G., a Hindu male, 36 years old, was admitted with a history of passing blood per rectum for about 6 weeks. Examination revealed rectal polyposis with perianal ulceration and a tender mass in the right iliac fossa. Fæces examination was positive for vegetative *E. histolytica*. During operation, three days after admission, a partially reducible ileo-cæcal intussusception was noticed and was resected. Blood pressure at the time of operation was 100/70 and hæmoglobin 60 per cent. The patient was discharged cured on 18th March, 1946, after a course of twelve emetine injections of one grain each daily. The rectal polypi had also disappeared.

Macroscopic and microscopic appearances—The intussusceptum could not be separated from the intussusciens due to adhesions and oedema. On opening the gut the apex of the intussusceptum was found covered by a raised gangrenous mass (figure 8, plate XXX). No ulceration was seen in the rest of the resected gut. Sections made from the vicinity of the necrotic area presented a combined pathology of amœbic and suppurative infection. Many amœbæ were present.

Case 6.—A., a Hindu male, aged 35, was admitted on 8th April, 1946, with acute pain of 3 days' duration in the right iliac fossa. On palpation, a tender mass was noticed slightly above the appendicular area. Fæces were not examined for amœbæ. During operation on 10th April, 1946, an easily reducible ileocæcal intussusception was seen. Since the nature of lesion causing intussusception was uncertain, a hemicolectomy was performed. The appearances of the lesion on opening the gut were characteristic of amœbic ulceration. Smears made from the ulcer were teeming with active *E. histolytica*.

Macroscopic appearances—The specimen consisted of the last four inches of ileum, cæcum and ascending colon with a hemispherical mass 2 inches in diameter formed by congested oedematous mucous membrane just beyond the ileocæcal junction (figure 9, plate XXX). The summit of the mass was ulcerated with tags of gangrenous material adherent. The rest of the mucous membrane was almost normal. Sections made from the periphery of the granulomatous mass showed necrosis of the mucosa and sub-mucosa with a few amœbæ, and acute inflammatory changes in the deeper layers of the sub-mucosa and the muscular coats.

An uncomplicated intestinal amœbic lesion is a non-inflammatory, necrotic ulcer. After

penetration of the mucosal glands the amœbæ colonize in the sub-mucosa and cause a colliquative necrosis there by elaboration of a cytolytic ferment. The initial spread of necrosis in the sub-mucosa is sideways with later extension to the mucosa which is shed, leaving behind a ragged ulcer with undermined edges. On rare occasions, the amœbic lesion seems to form a localized tumour producing sub-occlusion, a condition simulating tuberculosis, actinomycosis or a neoplasm. The chief factors, responsible for the production of a granulomatous mass, appear to be inflammation and oedema due to infection with secondary organisms. In the sections we have studied, these changes were prominent in the sub-mucous and muscular coats.

We feel, the granulomatous lesion while initiating occlusion does not by itself complete it, the intussusception and the increasing oedema thereby being the deciding factors. The irregular peristalsis initiated by the amœbic granuloma often results in acute intussusception, as noticed in the cases reported above, and hence our belief that without intussusception complete obstruction is unlikely to occur.

Diagnosis.—It will be seen from the cases reported that amœbiasis causing intestinal obstruction is not thought of as often as it should be. It may be profitable in tropical practice to remember that when a tumour mass is detected in the course of large intestine chiefly around the cæcum, a thorough examination should be made to eliminate amœbiasis; when fæces is not readily available for examination, a preliminary enema may be tried. Alternatively, the following procedure used extensively by one of us (D. G. R.) may be useful. Cotton-wool rolled round the tip of a 'kutchi' and soaked in saline is passed into the rectum, rotated gently and withdrawn. Smears made from this are examined for amœbæ.

Treatment.—Points requiring consideration are: (1) whether medical treatment in itself is sufficient in all cases; (2) if an operation is performed, whether resection of the gut should be done even when the intussusception is easily reducible; and (3) whether emetine should be started immediately after operation.

We feel, in cases of sub-occlusion, a condition difficult to diagnose, medical treatment in itself should be sufficient, but where intussusception has occurred causing complete obstruction and relief thereof is urgent but not feasible with medical treatment, resection of the gut is necessary. Resection seems to be essential even when the intussusception can be undone with ease, since there is a danger of recurrence as observed in case 4.

If resection of the gut is considered inadvisable due to the poor condition of the patient or for any other reason, a lateral anastomosis between segments of the bowel proximal and distal to the intussusception may have to be thought of. If resected, the gut should be opened and scrapings from the edges of the lesion examined for

E. histolytica with the minimum delay possible, if the amœbæ were not seen before operation. Gut resection should always be followed by a full course of treatment for amœbiasis bearing in mind there may be other lesions in the rest of the colon. Since most cases of intussusception show dehydration with low blood pressure and further deterioration in the general condition during operation, the advisability of immediate follow-up of emetine therapy has to be thought of. In such instances two alternatives are available: (1) Simultaneous administration of cardiac tonics with emetine with a periodic record of blood pressure and watch of cardiac rhythm. If the blood pressure tends to fall or the heart's action to be irregular the injections should be suspended. (2) Employment of amœbicidal drugs less toxic than emetine and its compounds.

Remarks

Though an attempt has been made to explain the pathogenesis of an amœboma, it cannot be said to be satisfactory. Every amœbic lesion in the gut is constantly exposed to bacterial infection, but it is only in a very small percentage of cases that this type of lesion is noticed. It may be due to a different strain of amœbæ or due to the secondary invaders gaining entrance into the sub-mucosa simultaneously and eliciting an acute massive inflammatory tissue reaction much ahead of the slow necrotic change effected by the amœbæ. Some useful information may be got by culturing the organisms in the material obtained from the interior of the granulomatous mass.

Summary

Six cases of amœboma (amœbic granuloma) of the large intestine are reported.

The significance of the secondary bacterial infection in the pathogenesis of amœboma is discussed.

The relative importance of œdema and intussusception in the production of obstruction is stressed.

EXPLANATION OF PLATES XXIX AND XXX

PLATE XXIX

- Fig. 1.—Case 1. Sausage-shaped intussusception mass with necrotic mucous membrane.
 Fig. 2.—Case 1. Low power photomicrograph showing submucous œdema and necrosis. The mucous membrane is lifted but not shed.
 Fig. 3.—Case 1. Medium power photomicrograph showing clusters of amœbæ in the muscular layer (upper half), and cellular infiltration (lower half).
 Fig. 4.—Case 1. High power photomicrograph of the amœbæ seen in figure 3.
 Fig. 5.—Case 2. Shows a raised circular mass just above the ileocaecal junction. A small ulcer 'A' is seen in the hepatic flexure.
 Fig. 6.—Case 3. Note the raised nodular mass 'B'.
 Fig. 7.—Case 4. Shows a hemispherical mass just above the ileocaecal junction. Œdema and gangrene are well brought out in the picture.

PLATE XXX

- Fig. 8.—Case 5.—Shows partially reduced intussusception. Note the apex 'C' of the intussusceptum.
 Fig. 9.—Case 6. Appearances resemble those in figure 7.

Difficulties in the diagnosis and the utility of a rectal swab examination for amœbæ are pointed out.

The indications for emetine therapy and gut resection are discussed.

Our thanks are due to the various surgeons of the Government General Hospital, Madras, for permitting publication of these cases.

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OBSERVATIONS ON YAWS IN BASTAR STATE

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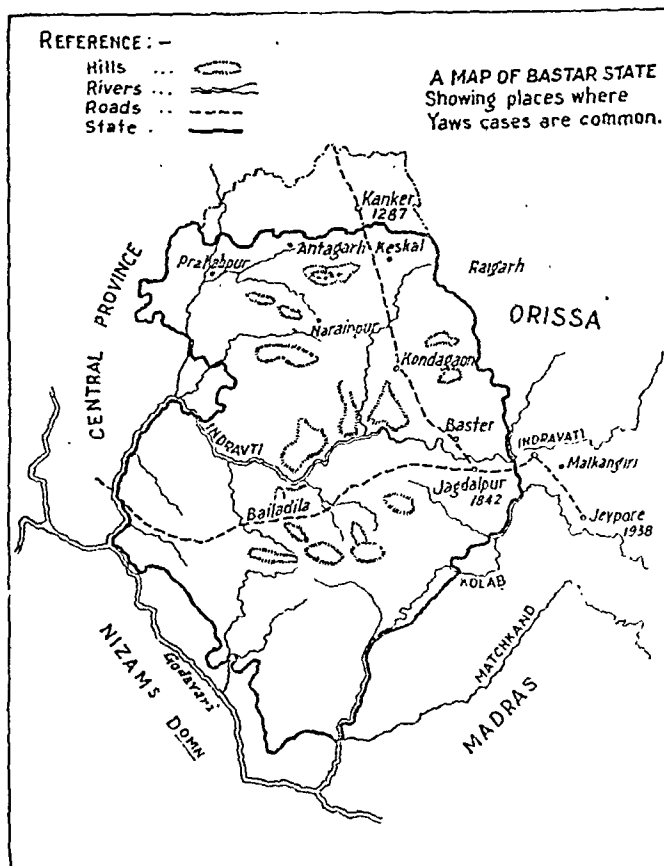
BASTAR is a Ruling State in Eastern States Agency. Its capital Jagdalpur is situated at a distance of 184 miles from Raipur (C.P.) and there is a metalled road connecting the two cities (see map). Although there is a distinct mention of yaws being a rare disease in India (Manson-Bahr, 1935), Bastar State appears to have a very heavy incidence—as a matter of fact yaws is one of the most common diseases in the State. Yaws, however, does not affect the better class of people or other people residing in the civilized areas of the State. It is essentially a disease affecting one class of aboriginals of the State, and that too, over selected areas. The 'Marias', as these aboriginals are called, are typical of the primitives who reside in the forests and at the foot of the hills, leading a rather quiet and peaceful life, in seclusion from other communities, and having completely different ways and means of living. They consume all sorts of animal flesh and a few vegetables, millets, etc. They have languages of their own—'Halbi' and 'Maria'—which others can hardly follow.

'Marias' all over Bastar do not have this disease, but only those residing in areas with an altitude of 2,000 ft. and above are affected. It is also prevalent on slopes and at the foot of the hills adjoining the above areas.

It is curious that 'Marias' do not have any venereal infection. Conversely, the civilized section and those living in the plains, amongst whom the incidence of syphilis is common, are free from yaws.

It is also worth mentioning here that yaws cases are seen in some parts of H.E.H. the Nizam's Dominions and in Malkanagri tahsil (in Koraput District in Orissa).

MAP



Clinical features of yaws as seen in Bastar State

It has not been possible to find out the exact incubation period of the disease due to extreme difficulty in eliciting a history from these aboriginal 'Maria' patients. Roughly the incubation period can be taken as varying between 3 and 4 weeks.

The difference between clinical features of yaws as described in standard books and those observed in yaws of Bastar State have been stated in a tabular form.

Illustrative case notes

Case 1.—Mura (see figure 1, plate XXX), 'Maria' male, aged 20 years, of good physique, presented himself for examination for the following :—

1. Papules, well raised over the surface of the body looking like excrescent nodules, were seen on the face, neck, back of the knee, and armpit. The papules were hard in feel. Originally these started as pimples and later developed into the present state.

2. One month before the appearance of these papules, the patient had fever and pain all over the body. On examination he had pain over the knee, wrist and elbow joints.

Kahn's test ++.

Three intravenous injections of neoarsphenamine (0.45 gm., 0.45 gm., 0.60 gm.) were given, one every fourth day. At the end of this course, all the papules and constitutional symptoms disappeared.

Case 2.—Nendo (see figure 2, plate XXX), 'Maria' female, aged 40 years, a rather

	Observations on yaws in standard books	Observations on yaws in Bastar State
1. Geographical distribution.	1. Described as a rare condition in India	1. A very common disease in Bastar State.
2. Native names ..	2. Parangi (Ceylon), Pururu (Malaya)	2. Gondi Roge, Sewai, Kachhi.
3. Age ..	3. Although two-thirds of the cases occur before puberty, no age is exempt.	3. It is by far common amongst the adult working class of ages between 20 and 40 years.
4. Sex ..	4. Three males appear to be infected to every female.	4. Practically of equal incidence in both the sexes.
5. Altitude ..	5. In Ceylon, yaws is a disease of flat low-lying districts, while practically absent from hill areas.	5. In Bastar, the 'Marias' living in areas with an altitude of 2,000 ft. and above, as also on the adjoining slopes of those high lands, are mostly affected. It rarely affects the other classes of aboriginals of Bastar State.
6. Symptom—pain ..	6. Rheumatic-like pain along with other constitutional symptoms in the primary and secondary stages of yaws.	6. Aching pain, deep inside the long bones, is a very prominent and in many cases the earliest symptom—long before the appearance of any other manifestation.
7. Attitude to treatment.	7. It is curious to note that, since the introduction of salvarsan, the natives of Congo are averse to receiving treatment till the secondary rash is well out.	7. 'Marias' of Bastar are quite alive to the sufferings from yaws and also the dramatic effect of a few injections in curing the malady. They are very prompt in coming up for treatment in very early stage and to get cured.
8. Gangosa and Goundou.	8. Mentioned in standard books	8. Conditions very rarely seen amongst yaws patients in Bastar.
9. Juxta-articular nodules.	9. Hard and fibrotic in feel	9. Not infrequently of cystic feel.

thin-built woman looking ill, presented herself for the following :—

1. Furfuraceous desquamated patches, suggestive of leucoderma on the upper surface of the chest (front and back), and the lateral surface of both the arms.

The patient states that about five months previously some pimple-like eruptions started in those areas and had itching. These later coalesced and burst to look like ulcers. She has now the desquamated patches only.

Four intravenous injections of neoarsphenamine (0.45 gm. to 0.6 gm.) one every fourth day were given. At the end of the course the lesions and the symptoms disappeared.

Case 3.—Buddhu, 'Maria' male, aged 50 years, had the following complaints :—

1. Acute pain throughout the day and night on both the knee-joints. Found difficulty in standing up after sitting. Could not flex the knees completely for 1 year.

2. Swelling and painful condition of the metacarpophalangeal and interphalangeal joints of the right hand. Restricted and painful movements of the above joints for 1 year.

3. Irregular leucodermic patches over the dorsal aspects of both the hands.

4. Juxta-articular nodule of the size of a small orange on the right knee. It was cystic in feel and painless.

5. Occasional fever and headache.

Kahn's test ++.

Three injections of neoarsphenamine (0.45 gm., 0.6 gm., 0.75 gm.) were given. At the end of the course the patient improved. Unfortunately the case could not be followed up.

Case 4.—Nago, 'Maria' female child, aged 2 years.

The child was brought down for the following complaints :—

1. Eruptions on the face. Mother of the baby said that the condition started as two small papules under the chin three months back, coalesced after one month and now looked like big ulcers.

2. Small circular healed ulcer (2 cm. diameter) showing desquamated scales on the back of the neck.

3. A depressed, fairly dry and shallow ulcer of oval shape, $\frac{3}{4}$ inch \times $\frac{1}{2}$ inch in dimension, just under the lateral end of the lower lip. There was a cracked slough in its centre and margins of the ulcer were everted.

4. One complete circular shallow ulcer looking like a ring, with its pale red granulating floor and everted margins on the right labia majora of the baby. Her temperature on examination was 100°F.

The patient responded to three intramuscular injections (0.15 gm. each time) of acetylarsan (M.&B.) given every fourth day, and was cured.

I take the opportunity of expressing my sincerest gratitude to my Chief, Dr. A. W. J. Morgan, for encouraging me in writing this article, to Major H. H.

Waynforth, District Engineer, Bengal-Nagpur Railway, for facilities of transport, to Captain W. P. S. Mitchel, the Chief Medical Officer, Bastar State, Jagdalpur, and to Dr. H. K. Roy.

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SODIUM ANTIMONY GLUCONATE IN THE TREATMENT OF INDIAN KALA-AZAR

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THE preliminary results of treatment of 50 cases of kala-azar and 2 cases of post-kala-azar dermal leishmaniasis were reported by the writers (Sen Gupta and Chakravarty, 1945) last year. Of the 50 cases of kala-azar treated, two died during treatment and 48 were discharged as clinically cured. The immediate results of this trial were quite satisfactory, the immediate cure rate being about 96 per cent, but it was emphasized that unless the relapse rate had been studied, accurate evaluation of this drug in the treatment of kala-azar would not be possible. In this paper it is proposed to present the results of the following up of the cases for a period of not less than 6 months after the completion of treatment, and to discuss the value of this drug in the treatment of kala-azar.

The patients who were either seen to be in good health or who wrote back saying that they were in good health, free from fever and splenic enlargement and that they did not require any further treatment for kala-azar, were regarded as permanently cured. All the patients (except one who was treated elsewhere) who relapsed came back and were either readmitted into the hospital or treated at the kala-azar out-patients' department of the School and the diagnosis was confirmed by serum tests and/or demonstration of the parasite. A fairly large proportion of the treated patients or their relations did not send any reply to the case follow-up questionnaire; these have been classified as 'untraced'. The result of the follow-up of the 48 cases discharged as cured is presented below :—

Permanently cured	..	21 cases
Relapsed	..	7 cases
Untraced	..	20 cases
Total	..	48 cases

It will be seen that only 28 cases could be followed up and of these 7 cases showed relapse. Thus it would appear that the relapse rate is

of the order of 25 per cent. But in view of the uncertainty about the rest of the patients and the fact that it has been our experience that when a patient had a relapse of kala-azar he usually came back to the hospital for treatment, it will probably be more reasonable to take the view that at least 7 in 48, i.e. about 15 per cent, showed relapse. Thus it would appear that the relapse rate is much higher than what was obtained with the older pentavalent antimonials of the urea stibamine-neostibosan group or with stilbamidine.

A brief analysis of the important data regarding the seven cases that relapsed is presented below :—

enlargement as an early case. The final figures then become as follows :—

Type of case	Total number	Cures	Relapses
Early	15	9	6
Well developed	13	12	1
TOTAL	28	21	7

This tends to show that the relapses are more frequent in the early cases than in the well-developed cases, though on account of the

TABLE I

Cases	1	2	3	4	5	6	7
Age in years	12	26	28	10	15	30	4
Weight (lb.)	55	(?) 109	90	45	67	97	27
Duration of illness in months	1½	10/30	10/30	3	2(?)	4	1
Size of spleen (in inches below 9th rib).	2	0	P	2½	½	2	2½
Aldehyde test	— ve	— ve	— ve	?	?	(+)	— ve
Sodium antimony gluconate:							
Total dose in c.c.	150	210	165	145	135	190	95
Relative total dose in c.c.	273	191	183	330	201	196	380

Also an analysis of the results of the aldehyde test in the whole group of 28 cases that could be followed up is presented below :—

TABLE II

Aldehyde reaction	Total cases	Cures	Relapses
Positive	12	12	0
Doubtful	4	3	1
Negative	10	6	4
Not done	2	0	2

From table I it will be seen that the total dose of sodium antimony gluconate used as well as the relative total dose per 100 lb. body weight was well within the limits that are regarded as optimum and as the injections had been given on consecutive days the treatment cannot be regarded so insufficient as to cause the relapses. Table II is helpful in assessing whether the cases were 'early' or 'well developed' and whether the duration of illness has anything to do with the occurrence of relapses. It is well known that the aldehyde test becomes positive usually when the disease is fully developed, and the duration is over three months, and that in 'early' cases the aldehyde reaction is negative or 'doubtful'. Thus 12 cases can be regarded as 'well developed' and 14 as 'early' cases. Of the two cases in which the test was not done, case 4 with duration 3 months and 2½ inches splenic enlargement may be regarded as a well-developed case and case 5 with duration (?) 2 months and ½ inch splenic

numbers being small the difference in relapse rate between the two groups is not strictly statistically significant.

In this connection it is necessary to consider the results of treatment of Indian kala-azar with sodium antimony gluconate by other workers using more or less a similar dosage scheme. These are presented below in a tabular form :—

Author	Number of cases	Relapses
Patel (1944)	6	0
Chakravarty (1945)	32	2
Sarma Chowdhuri (1946)	22	1
TOTAL	60	3

Thus only 3 out of 60 cases (i.e. 5 per cent) showed relapse in this collected group of cases. This figure is markedly lower than what has been obtained in our cases. It is thus necessary to further analyse clinical data of the cases of this combined group. From the protocols regarding the cases treated by these workers it appears that 2 out of 6 of Patel's and 5 out of Chakravarty's 32 cases may be classified as early cases; and that all the 22 cases of Sarma Chowdhuri were 'aldehyde-positive' well-developed cases of kala-azar. On adding this data to our results, the final results

of treatment of Indian kala-azar with sodium antimony^v gluconate work out as follows :—

Type of case	Total number	Cures	Relapses
Early	22	16	6
Well developed	66	62	4

It will be seen that in the early cases the relapse rate is of the order of 27 per cent ($27.3 \pm 2 \times 9.4$ per cent approximately) and in the well-developed cases it is about 6 per cent ($6.01 \pm 2 \times 2.9$ per cent approximately).

No strictly comparable data about the treatment of equally early cases of kala-azar with the older pentavalent antimonials are available at present. Napier (1932) however maintained that the early cases do not respond so well to treatment as the fully developed ones, and he presented evidence suggesting that relapses were more frequent in the early cases that were treated with one of the best of the pentavalent antimonials, *viz*, neostibosan.

As for the relapse rate after the treatment of well-developed cases of kala-azar with neostibosan, Napier (*loc. cit.*) found it to be 5.10 per cent. This is practically of the same order as what has been obtained with sodium antimony^v gluconate in the treatment of this type of cases (6 per cent).

Conclusions

On consideration of all the available data regarding the treatment of Indian kala-azar with sodium antimony^v gluconate it will be evident that the drug possesses considerable anti-kala-azar activity. The immediate clinical cure is obtained in approximately 96 per cent of cases of kala-azar. In about 4 per cent of cases the patient may fail to respond to treatment.

It is important to stress that the total dosage should on an average be 200 c.cm. of the solution containing 20 mg. of Sb. per c.cm. of solution for an adult, 150 c.cm. for a child, and about 75 to 100 c.cm. for an infant, in one course of injections given preferably on consecutive days, intramuscularly or intravenously.

On a study of the relapses, it has been found that the relapse rate is quite high, being of the order of about 27 per cent in the early cases of kala-azar treated with this drug. But as the final results of treatment of this type of equally early cases with the older pentavalent antimonials are not available at present, it is not possible to compare the results.

In the group of cases that has been classified as well developed, *i.e.* of duration more than 3 months and with a positive aldehyde reaction, the relapse rate of the cases treated with this drug is about 6 per cent—a figure which is not very different from what had been obtained with neostibosan in the past by Napier. In this

group of cases the permanent cure rate after subtracting the relapses and the failures is about 91 per cent. This also is not significantly different from the rate obtained with neostibosan by Napier.

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EPIDEMIOLOGY OF FILARIASIS IN CERTAIN PARTS OF H.E.H. THE NIZAM'S STATE

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THERE is no published record of the incidence of filariasis in Hyderabad State. Preliminary rapid surveys carried out in 1940-42 showed that the disease is endemic in a roughly kidney-shaped area, 4,800 square miles in extent, covering adjacent portions of Nizamabad, Medak, Karimnagar and Adilabad districts.

The endemic zone is situated between latitudes 18° and 19° N. and longitudes 78° and 79° E. The altitude is nearly 1,500 feet. The river Godavery flows through the northern portion and there are a number of irrigation tanks throughout. The climate is hot and humid, the temperature rising in summer to 112° F. and falling in winter to 74° F. The average rainfall is 35 inches. The area is indicated in the map.

The disease has also been recorded sporadically in other parts in the eastern half of the State.

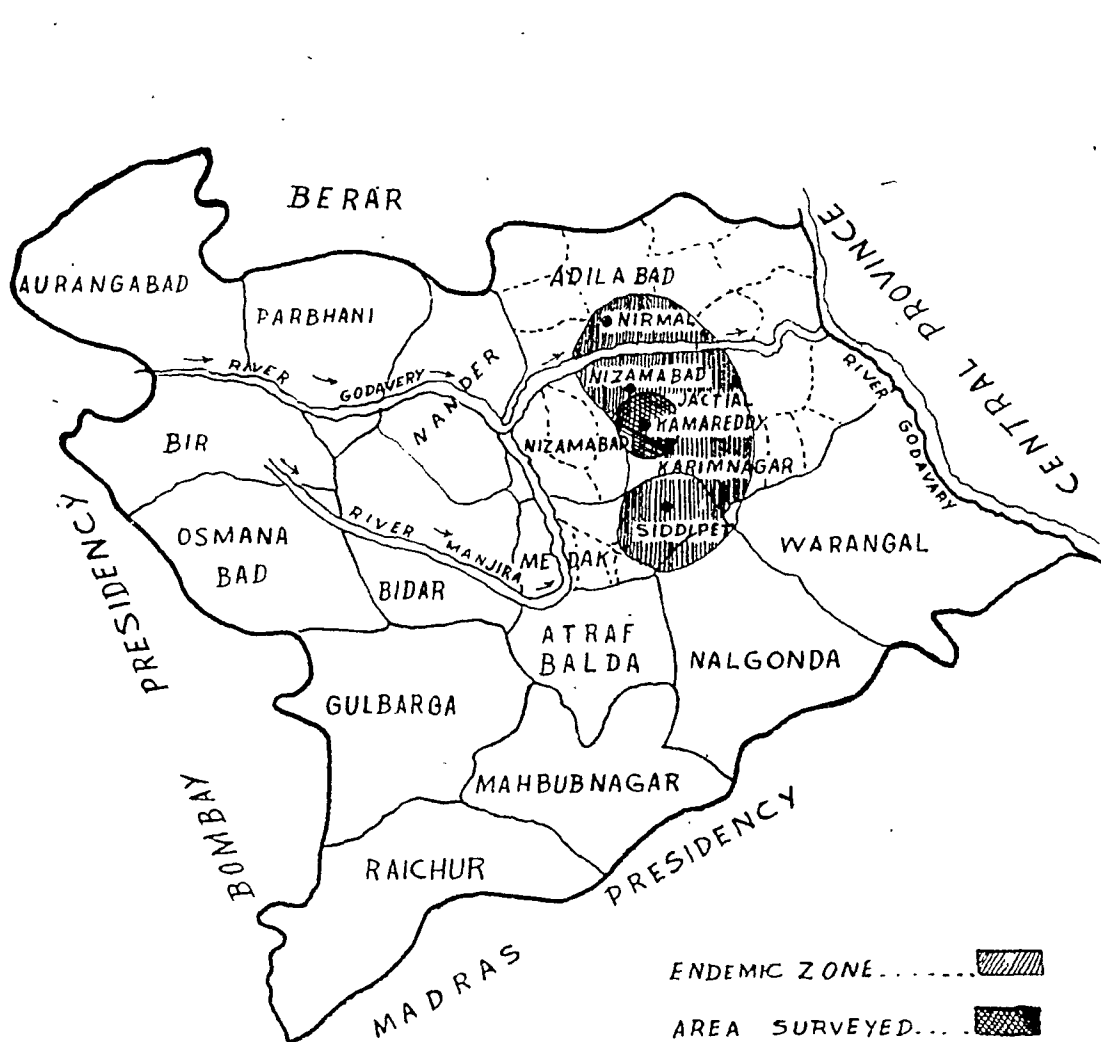
The present study was undertaken in 24 villages within a radius of 15 miles round Kamareddy town in the adjacent portions of Kamareddy and Sirsilla taluqs covering a population of 43,593. This area is shown heavily shaded within the endemic zone in the map. The study was primarily undertaken with a view to devising control measures against the disease.

Methods of Investigation

In order to determine the incidence of filarial disease and filarial infestation in a village, a house-to-house search was made of persons showing signs of lymphatic obstruction including lymphangitis. Thick smears of finger blood, approximately measuring 20 c.mm., were taken between 9 p.m. and 3 a.m. from diseased as well as healthy persons selected at random.

MAP

MAP OF NIZAM'S STATE SHOWING FILARIAL ENDEMIC ZONE



The total number of smears examined was 722 (see table II).

Filarial Disease Rate. Sex and Age Incidence

The result of the disease survey in the area is shown in table I. Sites affected and ages of patients were also noted.

Of the 692 cases recorded, elephantiasis of the leg accounts for 615 (88 per cent), of hand alone for 15 (2.16 per cent), of hand and leg for 35 (5 per cent), of scrotum alone for 20 (2.85 per cent), and scrotum and leg for 7 (1 per cent) cases. The highest disease rate of 4.9 per cent is in Gambhiraopet and the lowest 0.2 per cent in Kamareddy town where comparatively better sanitation prevails as it is the headquarters of the taluq. The average disease rate in the area surveyed is 1.6 per cent. There is no marked difference in incidence in either of the two sexes. The disease in the first age group is nil, and the

age group 46 to 50 accounts for the highest incidence, viz, 21.85 per cent. The earliest occurrence of lymphangitis was at the age of 7 in a boy in Ramareddy and that of elephantiasis of the leg in a girl of 8 years in Gambhiraopet.

Filarial Infestation Rate. Sex and Age Incidence

Of the 722 persons whose blood was examined for the presence of microfilaria, 545 were males and 177 females. Microfilaria were found in 92 persons giving an average infection rate of 12 per cent.

The first age group in both the sexes does not show any infestation. The seventh group 31 to 35 accounts for the highest infestation of 21.33 per cent. Infestation rate in the males is 13.3 per cent and in the females 10.16 per cent, so that there is no marked difference in the two sexes.

TABLE I

Serial number	Name of village	Population	ELEPHANTIASIS (INFLAMMATORY AND OBSTRUCTIVE)						Disease rate, per cent
			Leg	Hand	Hand and leg	Scrotum	Scrotum and leg	Total	
1	Dawanpalli ..	740	2	2	0.27
2	Lingapur ..	1,650	37	1	2	1	..	41	2.4
3	Krishnajiawadi ..	976	3	3	0.3
4	Chinnamallareddi ..	2,444	53	..	1	54	2.2
5	Rajampet ..	3,000	44	4	6	3	1	58	1.9
6	Sarampalli ..	462	3	3	0.6
7	Udloor ..	1,044	10	10	1.03
8	Yellareddi ..	2,909	8	..	1	9	0.3
9	Rameshwarpalli ..	354
10	Shabidipur ..	380	9	9	2.3
11	Eshanpalli ..	531	6	1	..	7	1.3
12	Mohsimpur ..	500	2	2	0.4
13	Uppalwai ..	998	4	4	0.4
14	Posanipet ..	1,190	11	..	1	1	..	13	1.09
15	Markhal ..	1,400	6	6	0.4
16	Kiasampalli ..	627
17	Takrial ..	732	3	3	0.4
18	Machareddy ..	1,361	16	1	1	18	1.3
19	Gambhiraopet ..	5,456	183	4	21	10	6	224	4.09
20	Nermal Camp ..	4,200
21	Bibbipet ..	3,727	101	3	2	106	2.8
22	Ramareddy ..	3,081	99	2	..	4	..	105	3.4
23	Kamareddy ..	5,300	15	15	0.2
24	Gungal ..	521
TOTAL ..		43,593	615	15	35	20	7	692	1.62

Infestation Rate among Persons with and without Elephantiasis

In table II data regarding infection, as determined by blood examinations in persons with

and without filarial disease in the individual villages surveyed, are presented.

The one feature common throughout, with the single exception of Ramareddy, is that the

TABLE II

Showing Infestation Rate among Persons with and without Elephantiasis

Serial number	Name of village	WITH ELEPHANTIASIS Number examined	Number with microfilaria	WITHOUT ELEPHANTIASIS Number examined	Number with microfilaria
1	Devapalli	25	3 (12.0%)
2	Lingapur ..	23	..	7	1 (14.2%)
3	Krishnajiawadi ..	3	..	2	1 (50.0%)
4	Chinnamallareddi ..	15	..	15	..
5	Rajampet ..	8	..	7	2 (28.5%)
6	Udloor ..	8	..	4	..
7	Yellareddy ..	5	..	7	..
8	Shabidipur ..	7	..	18	2 (11.1%)
9	Eshanpalli ..	2	..	22	4 (18.1%)
10	Mohsimpur ..	2	..	23	2 (8.7%)
11	Uppalwai ..	2	..	23	3 (13.0%)
12	Rameshwarpalli	10	1 (10.0%)
13	Posanipet ..	2	..	1	1 (100.0%)
14	Markhal ..	6	..	17	3 (17.6%)
15	Kasimpalli	26	2 (7.6%)
16	Takrial ..	3	..	22	2 (9.0%)
17	Machareddy ..	7	..	68	14 (20.6%)
18	Gambhiraopet ..	14	..	93	19 (20.4%)
19	Bibbipet ..	7	..	47	10 (21.2%)
20	Ramareddy ..	22	1 (4.5%)	56	5 (8.9%)
21	Kamareddy ..	2	..	66	10 (15.1%)
22	Nermal Camp	25	6 (24.0%)
TOTAL ..		138	1 (4.5%)	584	91 (15.5%)

infection rate in persons with apparent signs of filarial disease is zero; whereas high infestation rates are obtained in apparently healthy persons, the average rate being 15.5 per cent. The observations recorded by Iyengar (1938) in Travancore and Brown (1945) in U.S.A., in contrast to those of other observers in several parts of the world, also showed a markedly higher incidence of filarial infestation in individuals with no apparent manifestations of disease than in those showing evidence of disease. Our findings are not only in complete agreement with those of Iyengar (*loc. cit.*) and Brown (*loc. cit.*) but have gone a step further in that practically no filarial infestation was obtained in persons with filarial disease. On account of this contrariness in the incidence of filarial infestation and filarial disease in individuals, doubt has been thrown on the very basic theory of helminthic causation of the disease, although the remarkable coincidence of the geographical distribution of filarial infection and filarial disease furnishes evidence of the causal relationship between the two.

Endemicity Rate

In order that the endemicity rates obtained in different parts of India be comparable, it is necessary that their determination shall be made on a common basis. This is important in the case of filariasis as we have to base our findings on the fact that in addition to the cases showing evidence of disease a large number of asymptomatic cases with microfilaria in their blood have to be taken into account, and cases showing disease symptoms and microfilaria in blood not being counted twice. A tentative formula for the calculation of the endemicity rate is suggested below:—

$$E = \frac{d + \frac{i}{h}(p-d)}{p} \times 100$$

where 'E' is the endemicity rate expressed as a percentage of 'p' the population surveyed; 'd' is the number of persons showing signs of disease; 'i' the number of persons with microfilaria in the blood and 'h' the number of apparently healthy persons examined.

Calculated on the basis of the above formula the endemicity rate in the villages surveyed varied between 27.5 and 50 per cent with an average endemicity rate of 17.15 per cent for the whole area.

Average Infestation

This term denotes the average number of microfilaria per positive blood film, only one sample being taken from each person. The quantity of blood drawn was not actually measured but blood drops of uniform size approximating 20 c.mm. were taken as far as possible. The highest infestation recorded was 447 and the average rate for the area was 27.

Types of Filarial Infestation

The predominant infestation is *Microfilaria bancrofti* (Cobbold) which accounts for 92.4 per cent of the total infestation and *Microfilaria malayi* (Brug) for the remaining 7.6 per cent.

Mosquito Fauna

The following is a list of the Megarhine, Culicine and Anopheline mosquitoes caught and identified during the survey.

Megarhinini.—*Megarhinus splendens*.

Culicine.—(1) *Uranotania* sp. (2) *Aedomyia venustipes*. (3) *Ficalbia (Mimomyia) chamberlaini*. (4) *Mansonia (Mansonioides) uniformis*. (5) *Mansonia (Mansonioides) indiana*. (6) *Ficalbia (Ficalbia) minima*. (7) *Lutzia fusca-nus*. (8) *Lophoceraemyia minutissimus*. (9) *Culex fatigans*. (10) *C. vishnui*. (11) *C. bitaniorhynchus*. (12) *C. tritaniorhynchus*. (13) *C. fuscocephalus*. (14) *C. whitmorei*. (15) *C. mimulus*.

Anophelini.—(1) *Anopheles subpictus*. (2) *A. vagus*. (3) *A. culicifacies*. (4) *A. fluviatilis*. (5) *A. annularis*. (6) *A. pallidus*. (7) *A. hyrcanus*. (8) *A. barbirostris*.

Vector Mosquito

Of these mosquitoes collected *C. fatigans* was found to be the vector. Out of seven infected mosquitoes three showed shorter sluggish forms of larvæ in which herniation occurred on the slides after a few minutes, while in four mosquitoes full-grown and longer active larvæ of *Wuchereria* were found in the thoracic muscles and a few in the proboscis. The infection rate in *Culex fatigans* seems to bear a direct correlation with the filarial infection rate in man.

No specimens of *Mansonioides uniformis* or *indiana* could be found in the human dwellings even in places where *Mf. malayi* occurred. Search for these continues. Only a few adults were caught in the breeding places.

Breeding Places

At the time of the present investigation the *Culex fatigans* was found breeding only in cesspools and disused wells, although in the rainy season ubiquitous breeding places may be found such as collections of water in village-pits with decaying organic matter and ricefields manured with cowdung. The *Mansonioides uniformis* and *indiana* were found breeding in ponds containing *Pistia* at Gambhiraopet and in an old irrigation canal in Bibbipet originating from a big tank rich in aquatic flora including *Pistia* and *Marsillia quadrifolia*.

Conclusions

1. Although the filarial disease rate in any of the villages is not high, the endemicity rate in Machareddi, Gambhiraopet, Bibbipet and Nermal Camp are sufficiently high to call for immediate preventive measures. There is another group of a dozen villages with moderate endemicity rate which if neglected may further

deteriorate and might prove a great source of infestation to the surrounding villages.

2. Infestation and disease rates show no pre-dilection for either sex.

3. Earliest incidence of lymphangitis was found to be at the age of 7. The highest incidence of disease is in the age group (46 to 50) and the lowest in the (6 to 10) age group.

4. In agreement with the findings of Iyengar (*loc. cit.*) in Travancore and Brown (*loc. cit.*) in U.S.A. the filarial infestation rate in apparently healthy persons is very much higher than in persons showing clinical signs of disease in whom it is almost *nil*.

5. The importance of blood examination in determining the incidence of the disease in a given area has been stressed.

6. The predominant filarial infestation in the area surveyed is *Mf. bancrofti* and the vector is *C. fatigans*.

7. Malayi infestation has been detected and *Mansonoides uniformis* and *indiana* were found breeding in ponds and irrigation canals in which *Pistia Marsillia* grow.

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PLAGUE-MENINGITIS

By E. G. H. KOENIGSFELD

CAPTAIN, R.A.M.C.

and

K. P. S. NAMBIAR, L.M.P.

(Cantonment Hospital, Wellington)

THIS is a report on 2 cases of plague-meningitis observed by us among the comparatively small material of 41 instances of plague treated at Wellington, Nilgiris, in 1945-46.

We consider our cases worthy of record as the cerebro-spinal type of plague has been described in very few instances only, the disease being believed to be of extreme rarity.

Lewillon, Devignat and Schoetter (1940) reported in 1940 on plague causing primary meningitis. Unfortunately we have not been able to obtain their paper. Meyer of California, according to Manson-Bahr (1940), described a chronic relapsing meningeal form of plague, in which the patients exhibited meningeal symptoms and high fever. *P. pestis* was isolated in these

cases from the blood. Wu Lien-Teh, Chun, Politzer and Wu (1936) in a detailed review of plague comment with regard to the meningeal form that only rare instances of this kind have been observed. According to these authors one case was seen by Paso in 1925 in a Spaniard and another one by Lafort *et al.* in a native of Daker. The latter case showed *P. pestis* in the C.S.F.

As far as we can see no such cases have hitherto been described from this country.

Case Records

1. A woman, aged 47, from Coonoor, Nilgiris, fell suddenly ill with high pyrexia, malaise and subsequent delirium on 16th April, 1945. She was admitted to hospital where she developed a moderate enlargement of the axillary glands. A gland smear was taken, which on examination at the Pasteur Institute, Coonoor, was negative for *P. pestis*. She was treated with sulphonamides and iodine injections with the result that her condition showed considerable improvement within a couple of days. At the request of her family she was allowed to be taken home after a stay at hospital of less than one week. While at her home she continued to run an irregular temperature. On 6th May, 1945, one of us (Nambiar) was called out to see her as she had again felt very ill for the past 24 hours. At that stage she was found to be delirious and very restless. She vomited and retched incessantly. There was definite nuchal rigidity, and Kernig's sign was positive. The axillary gland had remained stationary without sign of impending suppuration. She was re-admitted to hospital where lumbar puncture was done. Culture of C.S.F. at the Pasteur Institute, Coonoor, showed *P. pestis*. The patient died the following day. She is reported to have been protected with anti-plague vaccine 2 months previously.

2. A girl, aged 7 years, was admitted to hospital on 7th April, 1946, for fever of 2 days' duration. On admission the child was apathetic, listless and markedly dehydrated. Eyes were sunken, not congested; the tongue was dry and coated. Spleen and liver were not palpable. Respiratory and circulatory system showed nothing abnormal. Left axillary glands were moderately enlarged and tender. Temperature 101°F. in axilla, pulse 128; gland smear examined at the Pasteur Institute, Coonoor, was positive for *P. pestis*. The patient was treated with sulphadiazine in full doses and intravenous glucose (25 per cent) 20 c.c. daily and fluids orally in abundance. On the 5th day of her stay at hospital she developed an inguinal bubo. The axillary glands supplicated and had to be incised. After this the patient appeared to be improving and the temperature returned to normal by 16th April. However, on the 21st, her condition became worse with a relapse of

fever and pains in all the joints. The left knee joint by then was swollen and inflamed. She was put again on sulphadiazine and the temperature settled again within 4 days with complete subsidence of the arthritis.

On 4th May, after one week of definite improvement, she complained again of headache and lost her appetite. Temperature rose again up to 102°F. that evening. From now onward her general condition, which was poor enough from the very beginning, deteriorated rapidly. On the following day she exhibited all signs of gross meningeal irritation. She vomited all the food given to her, showed marked head retraction and opisthotonos, and became delirious and restless. The pulse at that stage was thready and irregular.

In consideration of the fact that her condition after the long and debilitating illness was obviously hopeless we decided not to perform a lumbar puncture. During the following days, while she was gradually sinking, she became more and more apathetic, but the nuchal rigidity persisted and Kernig's sign remained positive. She died on 7th May.

Commentary

In the first case the diagnosis 'plague-meningitis' was confirmed by the findings of *P. pestis* in the C.S.F.

In our second case no lumbar puncture was performed and the diagnosis had to be made on clinical grounds. Even so there can hardly be any doubt that the symptoms were due to a genuine meningitis and not to mere toxæmic meningism. Head retraction and opisthotonos indicate severe meningeal irritation, which, in our opinion, can only be explained by an acute break-down of the blood-C.S.F. barrier, if not for the *Pasteurella* itself so at least for the toxins. We attribute equal significance to the vomiting which synchronized with the delirium and nuchal rigidity.

It was a striking feature of both cases that the meningeal signs occurred in the course of a prolonged illness after some initial improvement. Both patients seemed to respond favourably to sulpha drugs and succumbed only at a comparatively late stage of the disease. Sulphadiazine probably lessened the virulence of the germ to a certain degree, without rendering it entirely harmless, with the effect that the disease took a more chronic course and meningitis had time enough to develop. If this conclusion is correct more cases of plague-meningitis may be observed in the near future as sulpha drugs are now in general use in the treatment of plague.

There is still one question likely to be asked in connection with our cases: 'What is the appearance of the C.S.F. in simple, uncomplicated bubonic plague?'

We are not aware that systematic examinations of the fluid have been carried out so far,

and have, therefore, performed bacteriological tests and cell counts of the C.S.F. in our latest series of 5 cases of bubonic plague.

The results of all our tests have been entirely negative. Neither did the bacteriological examination of the clear C.S.F. show any growth of organisms on culture, nor was there any increase of the number of leucocytes. The intracranial pressure was normal.

Summary

Two cases of plague-meningitis have been described. One case has been confirmed bacteriologically by the finding of *P. pestis* in the C.S.F. The other case was diagnosed on clinical grounds.

A tentative explanation has been given for the occurrence of the disease and the possibility that more cases may be reported in future is pointed out.

No evidence could be obtained as to any change of the C.S.F. in uncomplicated cases of bubonic plague.

We wish to convey our thanks to Lieut.-Colonel G. S. Caithness, Wellington, for permission to publish this paper, to Lieut.-Colonel M. L. Ahuja, Director, Pasteur Institute, Coonoor, for kind permission to use the laboratory reports, and to Dr. D. I. G. K. Menon, for his advice and suggestions in writing this paper.

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SEROLOGICAL TECHNIQUE (contd.)

By S. D. S. GREVAL

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and

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DETERMINATION OF BLOOD GROUPS FROM STAINS

THE basis is the absorption of the known isonins by the unknown isogens of the stains proved to be caused by human blood only. The details are:—

1. A potent serum ab in which titre of a equals that of b is selected and its Minimal Dose of Equal and Simultaneous Agglutination, MDESA, determined, thus:

(d) A preliminary 3-slide test is carried out as follows :—

Suspension rbc A 1 vol.	Suspension rbc B 1 vol.
+	+
Serum ab 1 vol.	Serum ab 1 vol.
Suspension rbc A 1 vol.	Suspension rbc B 1 vol.
+	+
Serum ab 2 vol.	Serum ab 2 vol.
Suspension rbc A 2 vol.	Suspension rbc B 2 vol.
+	+
Serum ab 1 vol.	Serum ab 1 vol.

The agglutination should be equal and simultaneous. Otherwise the serum is rejected.

(b) The minimal dose of equal and simultaneous agglutination is determined next by dilution of the serum as follows :—

(i) With the standard capillary pipette add 1 drop of the serum to 1 c.c. of saline and draw a vertical line on the tube. This is a 1 in 50 dilution (approx.). Test two standard drops. If agglutination occurs in 2 minutes and is simultaneous and equal the dilution is further diluted to 1 in 100 (approx.) by adding 1 c.c. of saline to the same tube. The new dilution is tested as before.

(ii) If agglutination does not occur in a 1 in 50 dilution, one more drop of serum is added to the dilution and recorded on the tube by another vertical line. The balance of 1 in 50 dilution consisted of 49 drops. For all practical purposes the first drop of serum added to it was still in it. Another drop added means 2 drops of the serum in a total of 50 drops or a 1 in 25 dilution. The dilution is tested as before.

(iii) If no agglutination occurs in a 1 in 25 dilution, one more drop of serum, the third drop, is added to the dilution in the tube, which measures 48 drops. For all practical purposes the 2 drops of serum added previously are still in it. The dilution now is 3 in 49 or 1 in 16 (approx.). This dilution is tested as before.

(iv) If no agglutination occurs in a 1 in 16 dilution, one more drop of serum, the fourth drop, is added to the dilution which measures 47 drops. For all practical purposes the three previously added drops are still in it. The dilution now is 4 in 48 or 1 in 12.

(v) In the same way further addition of drops are made and stronger dilutions obtained. The outgoing drops, for testing, are looked upon as drops of saline only, the small quantity of serum in them being ignored. The dilutions corresponding to

1	50	
2	25	
3	16	
4	12	
5	9	
6	8	drops are 1 in
7	7	respectively.
8	6	
9	5	
10	4	
11	4	
12	3	

The dilutions are really slightly weaker than is shown.

The advantage of this method of titration is that although 13 dilutions (including the 1 in 100 dilution, not shown in the parallel lines of figures) are tested from each serum only one tube is needed. Four sera can be tested side by side in one Petri-dish. Limitation of space and the corresponding concentrations in observation result.

This scheme is slightly different from the one described earlier.

The weakest dilution causing an equal and simultaneous agglutination is the MDESA.

The simultaneity and equality may cease to exist at any dilution of the serum. The MDESA cannot then be determined.

The same cell suspension as used for determining the MDESA is used for the test proper.

2. Twenty-five milligrams of the stained cloth or 10 milligrams of scraped blood are left in contact with 0.1 c.c. of the serum dilution containing 3 MDESA in a unit volume (if a 1 in 16 dilution of the serum agglutinates an equal volume of 2 per cent rbc A and rbc B, the MDESA is 1 in 16; the dose is expressed as a dilution because the volume remains constant; 3 MDESA = 3 in 16; D denotes 'dose' or 'doses' as required) for half an hour at blood heat and overnight at ice-box temperature.

3. The serum dilution after contact is removed by centrifuging and tested for loss of isonins with the same 2 per cent known rbc A and rbc B. (i) If rbc A are not agglutinated the stain has absorbed the isonin a, the blood in the stain, therefore, was of group A. (ii) If rbc B are not agglutinated the blood in the stain was of group B. (iii) If neither rbc A nor rbc B are agglutinated the blood in the stain was of group AB. (iv) If both rbc A and rbc B are agglutinated the group of the blood in the stain was O.

MDESA may be replaced by MDSA provided the equality is perfect in a preliminary 3-slide test. The titration to determine the minimal dose is carried out as before. The two sides should show a distinct and simultaneous agglutination which may not be equal. The dose giving such a result is MDSA.

The following controls are put up : (1) Controls of rbc A and rbc B. There should be no pseudo-agglutination. (2) Controls of 3 MD(E)SA with suspensions of rbc A and rbc B. The degree of hæmagglutination should be of a high order. (3) Controls of 1 MD(E)SA with suspensions of rbc A and rbc B. The degree of hæmagglutination should be good. The control is specially important when working with MDSA only. The end result in the test proper should be like the control at least in equality. (4) Controls of unstained material, specially clothes. The hæmagglutination should not be affected. (5) Controls of bloodstains of known groups. The stains should be as old as or older than

those under test and should give the expected reaction.

The specimen from exhibits are examined after the controls have given the expected results. Only clear-cut agglutinations unaccompanied by \pm reactions are accepted. Otherwise 'the reaction is such that no opinion can be given'. Dilution of the absorbed fluid may abolish the \pm reaction.

Considerable failure to obtain results is acknowledged by workers in America. In India, the failure is even greater, probably due to more sweat and animal matter, which absorb isonins, in clothes.

Only the four blood groups can be determined satisfactorily from the stains.

Fæcal contamination destroys the isogens.

Determination of Group from Stains of Human Origin other than Bloodstains

Absorption with known isonins will also demonstrate the isogens A and B in the stains of saliva, nasal secretion and semen provided the subjects concerned are *secreters* (secrete the isogens in their saliva). Only a seminal stain can be identified as such. If such a stain absorbs one or both isonins the group of the subject is indicated as usual. In the case of non-absorption, however, the subject may either be non-secretor or belong to group O.

Blood Received from Distant Places for Grouping

The writers' laboratory requires the following: (1) About 0.25 c.cm. of blood dried as a stain on a chemically pure filter paper, not in the sun. An unstained part of the filter paper should also be available as a control. (2) About 0.5 c.cm. of clear serum in an ampoule. This is taken from a test tube in which about 3 c.cm. of blood have been put and allowed to clot *under sterile conditions* without disturbing the tube. (3) About 0.5 c.cm. of serum turbid with rbc in an ampoule. This is taken after shaking gently the contents of the tube, after the clear serum has been removed. The specimens are taken by a responsible medical man (preferably an official) and sent in a sealed and registered parcel. The impression of the seal is sent in another registered parcel.

The group is determined from the stain by absorption. The serum corroborates the finding. The rbc preserved in the turbid serum (if all has gone well with sterility) also corroborate the finding.

Opinion is withheld if a 'defective group' or an anomalous reaction is found. Fresh blood will be required for repeating the tests.

'Blood tests' for excluding paternity or maternity can also be performed on stains and serum, so far as the determination of blood groups goes. Opinion is withheld when (i) a defective group (ii) an anomalous reaction, or (iii) a combination incompatible with the

genetics of blood groups is encountered. Fresh blood will be required for repeating the tests.

DETERMINATION OF HETEROPHILE ANTIBODIES IN INFECTIOUS MONONUCLEOSIS (PAUL-BUNNEL REACTION)

The basis is the fact that a patient suffering from glandular fever develops in his blood antibodies which agglutinate sheep rbc.

Testing rbc.—Prepare a 2 per cent suspension in saline of washed sheep rbc 2 days old.

Unknown serum. From a suspected case of *infectious mononucleosis*.—Separate the serum from the clot and inactivate it for 30 minutes at 55°C. Make serial dilutions of the inactivated serum in geometrical progression 1 in 4, 1 in 8, 1 in 16, 1 in 32 and 1 in 64, thus:—

(1) Take five test tubes (4 inches length and $\frac{1}{2}$ inch breadth) marked 1, 2, 3, 4 and 5. (2) Add 1.5 c.c. of saline to tube marked 1 and 1 c.c. to each of the other four tubes. (3) Add 0.5 c.c. of serum to the tube marked 1 and mix. This is 1 in 4 dilution. (4) Take 1 c.c. of the dilution in a pipette from tube marked 1 and add to the tube marked 2 and mix. This tube now contains 2 c.c. of 1 in 8 dilution. (5) Repeat the process from tube marked 2 to tube marked 3 and so on till the tube marked 5 is reached from which 1 c.c. is rejected. All the five tubes now contain 1 c.c. of the serial dilutions stated above. Results will be recorded in terms of these initial dilutions.

If sera left over from a Wassermann reaction are to be used the first dilution 1 in 4 may be discarded. The second dilution is made from the usual 1 in 5 dilution (usually made for the Wassermann reaction) thus: Take 5 volumes of the 1 in 5 dilution and add 3 volumes of saline. The resulting dilution is 1 in 8. Proceed as before.

Setting up tests.—(1) Distribute 0.5 c.c. of the dilution from each tube to another set of 5 tubes in a rack. (2) To each of the tubes containing 0.5 c.c. of a serial dilution of the serum add 0.5 c.c. of the 2 per cent suspension of sheep cell. (3) Also add 1 c.c. of normal saline solution to each of the tubes making a total volume of 2 c.c. in each tube. (4) Shake and place the rack containing the test tubes in water bath at 38°C. (air incubator at 37 will also do) for 1 hour. (5) Leave in ice-box overnight. (Refrigerator recording 2°C. to 8°C. temperature will do.)

Reading the results.—Next morning invert each tube 3 times with its mouth covered by a cork (finger tip instead of the cork, in the original method, is not recommended) and read the degree of agglutinations as follows:—

Firm disc	+++
Disc easily broken into large flakes	++
Fine agglutination	+
Barely perceptible but definite agglutination	\pm

Evaluation of result.—A titre of 1 in 64 (initial dilution) is diagnostic. A \pm reaction is to be taken as indicative of titre.

Only (1) aplastic anæmia and (2) serum sickness are known to interfere. Blood films and history will exclude them.

The interfering antibody present in the blood of cases of serum sickness can be absorbed by

a suspension of guinea-pig kidney. It is hardly necessary.

Even a titre of 1 in 32 may be significant.

The reaction is not constant. Outbreaks of glandular fever in which the 'reaction was almost uniformly negative' have been described.

To be continued.

A Mirror of Hospital Practice

A CASE OF LEIOMYOMA CUTIS

By D. PANJA

and

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AN Indian male, aged 38 years, was admitted for painful cutaneous nodules on the body.

History.—About 16 years ago the patient first noticed a small hard nodule in the right axilla. Soon after, a few nodules appeared on the left buttock. These were small, hard and movable with the skin. A few years later some more nodules appeared in different parts of the body. These nodules were painless for the first few years, but recently these became very painful for which medical help was sought.

His family history was of no importance.

Present condition.—The patient's general health was good. There were groups of nodules in the lower lumbar region of the back, right scapular region; a few on the right cheek (see figure 1, plate XXX), two on the right axilla and three on the left buttock. The nodules were of different sizes varying from a pin's head to a small nut; the smaller ones were of dull red-dish colour and the larger ones of skin colour. The nodules were hard and movable with the skin and very painful on pressure or even on gentle manipulation.

The patient complained of excruciating pain coming in paroxysms, especially at the time of defæcation and micturition. Even a sudden change of temperature or blow of wind would bring such paroxysms of pain.

No abnormality was detected in the urine and blood count.

W.R. and Kahn test were negative.

Clinically the nodules looked like those of neurofibromatosis of von Recklinghausen.

Histopathology.—(Figure 2, plate XXX) 'Practically the whole nodule consists of dense masses of interwoven bundles of smooth muscle fibres distributed throughout the cutis extending

down to the subcutaneous tissue at the centre and in some places invading the papillæ and obliterating them. The nuclei of the muscle fibres have normal rod-shaped characters and are embedded in finely fibrillated protoplasm with no demarcation between the various cells. The bundles have been cut in all directions giving the interlacing characters and their divers course throughout the growth. In the centre the bundles are dense and have replaced all other structures except the capillaries which show certain amount of endothelial proliferation and a perivascular infiltration. The lymphatic spaces are markedly dilated and surrounded with mononuclear leucocytes. The muscular tissue is free from elastic fibres which are abundant in the surrounding tissue. Diagnosis—Leiomyoma'.

Therapeutic Notes

A HUNDRED YEARS OF ANÆSTHESIA (1846 to 1946)

By S. K. SARKAR, M.B.

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PRIESTLEY is credited with the discovery of nitrous oxide in 1772 but its analgesic properties were first indicated by Davy in 1799. In 1800 Davy published his reports on this gas which included the following statement:—

'As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place.'

In 1806 Serturmer isolated morphine, the chief alkaloid of opium. Magendie prescribed this medicine by mouth in 1820. This was the first administration of a narcotic in known doses.

Henry Hill Hickman followed up Davy's researches, and in 1824 published a pamphlet



Fig. 1.—Case 1.



Fig. 2.—Case 1.



Fig. 3.—Case 1.

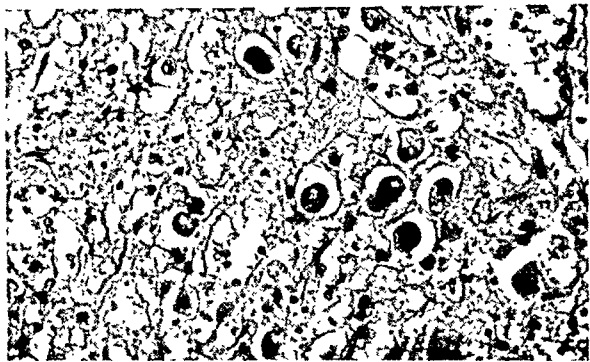


Fig. 4.—Case 1.



Fig. 5.—Case 2.



Fig. 6.—Case 3.



Fig. 7.—Case 4.

BIC GRANULOMA (AMOEBOOMA) OF THE LARGE INTESTINE :
 DIVINDA REDDY & C. MOHAN RANGAM. (O. A.) PAGE 463

OBSERVATIONS ON YAWS IN BASTAR STATE :
 AMULYA CH. SEN GUPTA. (O. A.) PAGE 466



Fig. 8.—Case 5.

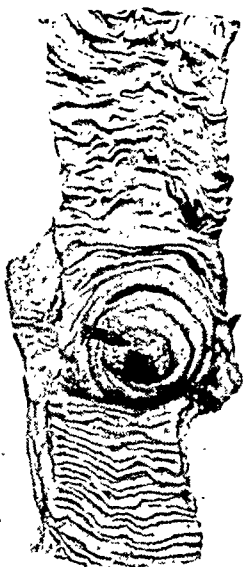


Fig. 9.—Case 6.



Fig. 2.—Case 2. Note the furfuraceous desquamation looking like leucodermic patches on the arms and chest (secondary stage).



Fig. 1.—Case 1. Note the primary papules looking like nodules on the forehead and just above left clavicle on the neck (primary stage).

A CASE OF LEIOMYOMA CUTIS : D. PANJA & L. M. GHOSH. (M. H. P.) PAGE 478



Fig. 1.



Fig. 2

where he clearly formulated his belief that surgical anæsthesia could be attained by inhalation of certain gases. He experimented with different gases but most of his work was on carbon dioxide. In the light of recent work of Haldane the choice was unfortunate. Nevertheless, he deserves recognition as the first to define clearly the principles of inhalation anæsthesia.

In 1844 Horace Wells became interested in nitrous oxide anæsthesia. In January 1845 Wells, with his partner Morton, demonstrated the administration of N_2O on a patient who came to have one of his teeth extracted. The attempt failed, anæsthesia being most inadequate and the patient suffered considerably.

Morton, however, did not lose faith and he continued his investigation with the possibility of producing anæsthesia by nitrous oxide and other inhalation vapours. In 1846 he administered ether at the General Hospital, Massachusetts, on a man who was operated upon for a congenital tumour on the neck. The anæsthesia was an unqualified success. This is claimed to be the first surgery under general anæsthesia and credit must go to William C. Morton, although Dr. Jackson, a chemist, also claimed the credit since it is alleged that he had suggested its use to Morton. It is also said that Crawford W. Long (1815 to 1878) had used ether earlier in 1842 in a few minor surgical procedures in the U.S.A. but he did not pursue his discovery much further.

In 1847 Simpson discovered the use of chloroform.

In 1862 Colton re-introduced N_2O , against formidable opposition, by demonstrating its use on an old lady; he successfully extracted a few teeth without pain under nitrous oxide inhalation.

Although John Snow (1813 to 1858) did not have any original discovery to his credit, he was the first to appreciate the urgent need of physiological research. It was Snow who set the seal of propriety on anæsthesia in obstetrics. After Snow's death the only important worker was Clover (1825 to 1882). He is best remembered by his ether inhaler. He was the first to suggest and make practicable a nitrous oxide ether sequence. By this, not only was the unpleasantness of an ether induction avoided but also universal use of nitrous oxide was made possible.

There was very little progress in anæsthetic technique until the 20th century. World War I was responsible for the more general adoption of the endotracheal technique although it was suggested by Trendelenburg as early as 1869. It was not until 1917 that endotracheal anæsthesia for soldiers, needing surgery of the head and face, was widely adopted. To Rowbottom and Magill must be given the credit for simplifying the technique.

Since 1921 various derivatives of barbituric acid have been used as basal anæsthetics with

varying success but this group of drugs did not attain universal popularity till 1932 when Reinhoft first used evipan clinically in Germany.

Pentothal sodium was introduced by Lundy in the U.S.A. in 1934. Evipan was first reported in Great Britain by Jarman and Abel in 1933, who also introduced pentothal in 1936.

The anæsthetic properties of di-vinyl ether or vinesthene were discovered by Leake and Chen in 1930. The popular sponge-filled inhaler was designed by Colonel Victor Goldman who until recently was in this country. Vinsthene is also now being used as a supplement to gas oxygen.

The anæsthetic properties of cyclopropane were discovered by Lucas and Henderson in 1929 but it was clinically developed by Ralph Waters of Madison in 1933. Incidentally, he is also credited for the technique of carbon dioxide absorption which made use of expensive gases like cyclopropane a feasible proposition. A new circle type of absorber was introduced by Dr. William Mushin in an article to the *British Journal of Anæsthesia*, January 1943.

In July 1943 Dr. Langton Hewer submitted to the medical press his reports on 4,000 administrations of trichlorethylene (trilene). Its use is now confined mainly to analgesia in obstetrics although its usefulness as a supplement to N_2O and oxygen for Cæsarcan section has also been reported.

During World War II many advances must have been made in the art of anæsthesia, full reports of which are not yet available, but it is noteworthy that ether and nitrous oxide, the first two gaseous anæsthetics to be discovered, have retained their popularity and their use has not been challenged despite the introduction of many other anæsthetics.

NOTES ON SOME REMEDIES

III. QUININE

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We have included this old and common drug in this series, not that we have much new to say, but because we feel that there is still scope for laying stress on certain points that are sometimes overlooked or neglected in practice particularly the relative importance of quinine as compared with other antimalarial drugs. This necessitates inclusion of some details, though these must be familiar to many practitioners.

The therapeutic effects of cinchona bark are due to the amorphous and crystalline alkaloids that are present in it. The amorphous ones have

a poor antimalarial action, while of the four crystalline alkaloids quinidine has a depressant action on the heart, cinchonine in large doses is liable to cause gastro-intestinal irritation and cinchonidine is comparatively weak. Quinine is therefore preferred and used as one or other of its salts, the sulphate being the one which is most frequently given by mouth, while the hydrochloride, bihydrochloride and dihydrobromide are used for injections. The ethyl carbonate (euquinine) being insoluble and tasteless is often, if available, preferred for children, but as it is not fully absorbed, a higher dose has to be prescribed, 8 grains of it roughly corresponding to 5 grains of the sulphate.

Cinchona febrifuge, a mixture of all the alkaloids, is cheaper than quinine and almost equally efficacious—some say it is better than quinine in vivax infection—but as it is not standardized, some samples being potent and others almost inert, the Malaria Commission of the League of Nations recommended a substance called totaquina which shall contain not less than 70 per cent of crystalline alkaloids of which 15 per cent must be quinine. No cinchona febrifuge should be used which does not comply with this standard. It is now included in the B.P.

Action on the parasites

Given by mouth, quinine is rapidly absorbed chiefly from the small intestine and appears in the blood within 15 minutes, reaching its maximum concentration in a few hours. It remains in the blood for a short period only and in minute traces not sufficient to have any direct action on the malarial parasites. A large proportion of it is deposited in various organs including the liver where it is mostly destroyed, and much of the remainder is excreted unchanged in the urine, starting within half an hour of administration and being completed within 24 hours. Intravenous injection gives immediate high concentration followed by rapid fall, it is fixed in the tissues and later returns to the circulation. Given intramuscularly it is fairly rapidly absorbed, but occasionally it is held up in the muscles either from defective blood supply of the injected part or from bleeding in the tissues caused by the injection.

The action of quinine on the parasites is probably an indirect one by stimulation of the natural defences of the body, but its exact nature is not known. It has no action on the sporozoites injected by the mosquitoes and acts best on the asexual forms in the peripheral blood. Its action is slight on the gametocytes of *Plasmodium vivax* and *malaria*, while it has no action on the gametocytes of *P. falciparum*.

In acute attacks

To control the clinical manifestations of the disease small doses of quinine are sufficient, large doses produce no greater therapeutic result but

merely exert a toxic influence on the patient. Ten grains of the sulphate or cinchona febrifuge are given two times a day after food (three times a day for first three days in falciparum malaria). It is a mistake to recommend one of the more soluble salts such as the bisulphate or bihydrochloride on the plea that it is on account of the greater solubility more easily absorbed since all salts of quinine are reduced to the base in the duodenum before absorption into the blood stream. For women and weak men the dose may be reduced to $7\frac{1}{2}$ grains. Children tolerate quinine well and need relatively larger doses; the dose in grains is calculated as 1 to $1\frac{1}{2}$ plus half the age of the child in years and is best given in treacle or honey. Some clinicians prefer to spread the dosage over twenty-four hours so as to keep the concentration in the blood more or less constant. It used to be taught that the parasites are most easily destroyed by quinine when they are free in the circulation, and it was customary to give it 2 or 3 hours before the onset of the expected paroxysm. Whether this view is correct or not, it is better to maintain a regular dosage. There is no basis whatever for the popular belief that quinine should not be given during fever. In most cases the parasites quickly disappear from the blood and the fever ceases within 3 to 4 days, but the treatment should be continued for at least 5 days after the fever subsides, the total course usually lasting 7 to 10 days. A second course after an interval of 10 days has been recommended in falciparum infection. The quinine should be given in solution. Tablets are uncertain as they may not be dissolved in the alimentary tract. If for any reason they must be given, the more soluble salts such as the hydrochloride or bisulphate are preferable and are better allowed after the fever is brought under control.

Causes of failure

If quinine is properly administered and absorbed it is bound to cure most of the patients. Failure to obtain the desired result may be due to its absence or shortage in the mixture because of the dishonesty of the dispenser or the manufacturer. This can be detected by a simple test.* Quinine is not infrequently adulterated with

** Test for quinine in mixtures.—*

- (1) Take 2.5 c.c. of the reagent (prepared by mixing pure phosphotungstic acid $\frac{1}{2}$ oz., dilute sulphuric acid $2\frac{1}{2}$ oz., and rectified spirit 6 oz.) into each of two narrow tubes.
- (2) Add to one 0.25 c.c. of the quinine solution to be tested and to the other 0.25 c.c. of a control mixture (*viz.* 10 grains to the ounce). Mix thoroughly.
- (3) Stand the two tubes in a rack, and compare the heights of the precipitates settled at the bottom. Any gross deficiency is easily observed.

N.B.—Two pipettes—one marked to measure 2.5 c.c. and another 0.25 c.c.—may be used for convenience.

lime, starch and other inert substances. The tablet may be insoluble through the presence of too much amorphous alkaloids or because it may have a coating quite impervious to water. There are some patients who deceive their doctors by deliberately not taking the medicine for some reason or other. Some authorities have suggested that certain strains of malaria parasites may become 'quinine resistant' after prolonged medication but there is very little evidence to support this hypothesis. There is a simple and useful test for quinine in the urine.* If this is not positive during quinine administration, the attack will not respond, either the patient is evading the drug or his absorption is defective. Vomiting or other gastro-intestinal disturbances are the usual causes for non-absorption.

Parenteral therapy

This is unnecessary as a routine measure, and never as an alternative to the oral route, but essential in certain circumstances, as in severe types of falciparum malaria with or without unconsciousness. It is especially indicated when quinine cannot be swallowed or its retention is doubtful as in nausea and vomiting. In such cases it has been found that even a single injection may have the desired effect and enable the patient to take and absorb quinine by mouth. If necessary it may be repeated after six hours, but parenteral therapy should not be continued longer than is necessary. A third dose is rarely needed. The intravenous route should be more often employed, and indeed there are many clinicians who always prefer it to the intramuscular method.

Intravenous injection.—This is especially indicated in severe and urgent cases, e.g. algid and cerebral malaria, where a very rapid concentration of the drug in the blood stream is considered advisable. Five to ten grains of quinine dihydrobromide or bihydrochloride are dissolved in 20 c.c. of normal saline or glucose solution and injected slowly in the vein at the bend of the arm at a rate of about 2 to 3 c.c. per minute. In view of the possibility of a sudden fall of blood pressure adrenaline should be kept ready at hand. In an emergency, if no sterile diluting fluid is available, the quinine solution is drawn in the syringe, and after inserting the needle into the vein, diluted with the patient's own blood and then injected slowly as usual. This is not the place for discussing concomitant treatment, but the necessity of treating the accompanying dehydration must be pointed out.

* *Test for quinine in the urine.*—

Add a few drops of the reagent (prepared by mixing 1.45 grammes of mercuric chloride in 80 c.c. of water with 5 grammes of potassium iodide in 20 c.c. of water, agitating the solution all the time) to 5 c.c. of urine. A precipitate forms if quinine is being excreted in the urine. If albumin be present in the urine, it should be boiled and filtered while warm.

Too often are its manifestations of weakness, feeble pulse and low blood pressure mistakenly ascribed to toxæmia. When the patient is in collapsed condition, it would be advisable to increase the amount of saline. Intramuscular injections of quinine are not desirable in such cases as most probably it will not be absorbed properly in the failing state of circulation.

Intramuscular injection.—Ten grains of quinine hydrochloride or bihydrobromide are dissolved in 2 to 4 c.c. of sterile water with, if possible, 5 grains of urethane which acts as an analgesic. Quinine bihydrochloride, though more soluble, makes a very acid solution and causes pain when injected. The best situation for injection is into the gluteus maximus, care being taken to avoid the sciatic nerve or the iliac bone and not to inject into the subcutaneous tissue as this will cause pain and stiffness. Any part of the buttock that can be seen, when the patient is sitting, is free from danger of injuring the nerve, but of course the injection should be made in the recumbent position only. The drawbacks to intramuscular injection are that it is apt. to be painful and leave indurations that may last for a long time. There is usually some local necrosis which may lead to abscess in debilitated individuals. Tetanus, due to introduction of spores at the time of injection, is rare. The intramuscular injection is the method of choice in young and fat people in whom veins may not be visible.

Relapses

The antimalarial drugs can control acute attacks but they cannot eradicate the infection in the body; sooner or later when the drugs have been discontinued the parasites may begin to multiply again causing a relapse. While quinine has undoubtedly some influence on it, a relapse rate as high as 50 per cent is to be expected if no other drug than quinine is used in the case of benign and to a less extent in quartan infections. Relapses are relatively uncommon after malignant tertian infection, no matter what antimalarial remedy is used. The cause for this is not clearly known. Formerly it was the practice to give long courses of quinine in large daily doses with the idea that relapses might thus be prevented or at least their incidence materially decreased but it is now realized that such courses influence the rate but little. There is good reason for believing that the final eradication of malarial infection is brought about by an immunological process as a result of relapses or repeated infections but the exo-erythrocytic cycle of the parasites on which investigations are now proceeding may throw fresh light on the subject.

Quinine in special cases

As mentioned above, in cerebral and algid forms of malaria intravenous injection is to be

preferred. Ten grains of quinine are first given and further injections may be given if necessary in 6-grain doses every 4 to 6 hours until the patient is able to take it by mouth.

Quinine does not act as an oxytocic in pregnancy complicated with malaria, provided labour has not already commenced. The disease itself, especially falciparum infection, is more likely to produce abortion than quinine and may even infect the fœtus. Small doses are given such as 4 or 5 grains three times a day. A bromide mixture may also be given and the patient should be in bed. In debilitated and anæmic women quinine acts more powerfully on the uterus and is better avoided. Quinine given parenterally is said to be more liable to produce abortion in these women. Whenever possible it is best to give mepacrine in pregnancy.

In malarious villages patients are often seen with hard considerably enlarged spleen and anæmia with or without fever. Ordinary quinine treatment has little or no effect. Their improvement depends on the development of immunity aided by nourishing food, tonics and small doses of quinine. Hæmatinics such as iron and liver extract injections are also useful.

Quinine in suppressive treatment

Quinine is a useful prophylactic and will keep a person free from clinical malaria even in a very malarious place. The freedom lasts as long as the drug is continued and is often followed by a clinical attack. When a non-immune or a casual visitor goes to a malarious place, he should take 6 grains quinine daily and continue taking the daily dose for two weeks on leaving the locality. Tablets here are preferable as the bitter taste of the mixture deters many from taking it regularly. As quinine is not stored up in the body, there is no advantage as in the case of mepacrine, in giving it in advance prior to arrival in the infected place. The indigenous inhabitants or permanent settlers in a malarious country should not depend on drugs but take other measures to prevent malaria; they will have periodical attacks which are treated, and at the same time become more or less immune.

Toxic effects

The administration of quinine in therapeutic doses is attended with little or no risk. Certain side effects may however be encountered in practice. Transient slight deafness, buzzing or ringing in the ears, mental depression, giddiness, sense of fullness in the head, or headache are common, but are of little importance and subside rapidly when the drug is discontinued. These are attributed to cinchonism caused by the action of quinine upon the central nervous system. In very large doses the circulatory system is depressed; there may be marked and

persistent deafness and loss of vision. Quinine amblyopia is said to be caused by spasm of the retinal artery. Occasionally quinine acts on the body tissues generally and may give rise to anaphylactic-like symptoms, viz, urticaria, hæmorrhages or hæmoglobinuria, resembling blackwater fever. Sometimes the untoward symptoms appear even after small doses owing to idiosyncrasy to the drug.

Quinine, mepacrine and plasmochin

We shall conclude this article by briefly referring to the relative uses of these drugs, as some confusion still exists in the minds of some practitioners. Quinine and mepacrine have much the same action on the malarial parasites and the same limitations. Both are useful in the treatment of acute malarial attack. Neither of them can be relied on to prevent relapses in benign tertian malaria following the discontinuance of therapy, although the interval between the attacks is said to be longer with mepacrine treatment. Mepacrine if properly given practically always suppresses the malignant form of malaria while the action of quinine is less certain in this respect. With proper administration mepacrine is no more liable to cause serious toxic effects than quinine is. As it is excreted slowly from the body; it retains its therapeutic effect for a longer time after cessation of treatment and its comparative tastelessness gives it a valuable advantage in malaria prophylaxis. It can be given in blackwater fever and pregnancy and those with idiosyncrasy to quinine can take mepacrine with impunity. Some think that its action on the initial pyrexia of the malarial attacks is slower than that of quinine and prefer to give a preliminary two days' course of quinine before commencing mepacrine.

Plasmochin, on the other hand, differs from both quinine and mepacrine and can never be used as a substitute for them but rather to supplement their action. Being a very poor schizonticide, it has little or no action on the acute malarial attack and should never be used in the treatment of such an attack. But it has a marked gametocidal action, especially on the crescents of malignant tertian malaria (which are not affected by quinine or mepacrine), and as the gametocytes spread the infection through mosquitoes plasmochin helps in general prophylaxis. A more important action of plasmochin is its reducing effect on the relapse rate, especially of the benign tertian malaria. It should be given along with quinine in doses of one tablet 0.01 gm. twice a day for 3 to 5 days preferably after the fever is controlled. Plasmochin is a toxic drug and should be administered under medical supervision. Mepacrine and plasmochin should not be given together, concurrently or in separate doses, as thereby their toxic effects are enhanced. It should be started two days after the completion of the mepacrine course.

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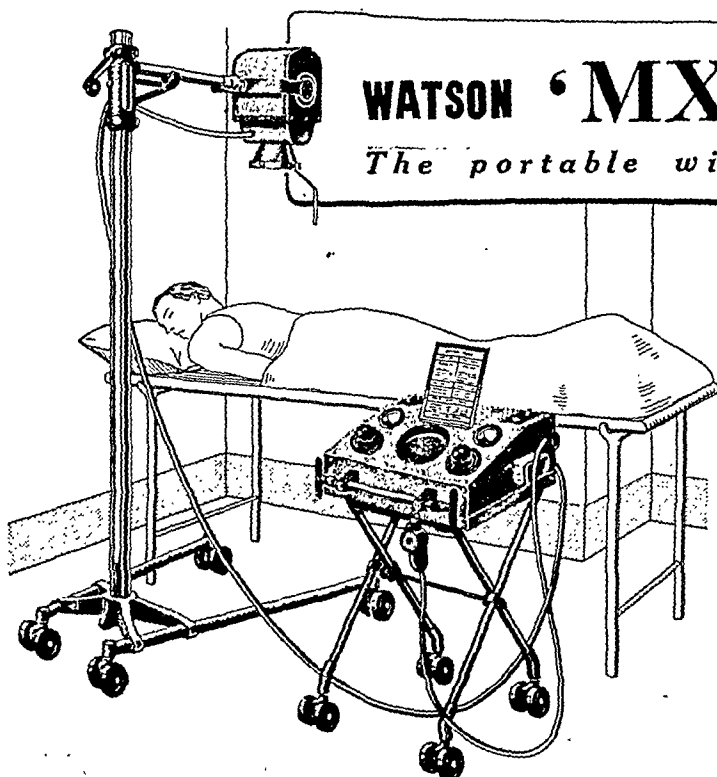
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Indian Medical Gazette

NOVEMBER

POWER AND PROCEDURE OF THE GENERAL MEDICAL COUNCIL OF GREAT BRITAIN AND IRELAND, AND THEIR INFLUENCE ON INDIAN MEDICAL AFFAIRS

THE Medical Council of India and the Provincial Medical Councils follow closely the General Medical Council of Great Britain and Ireland, and are likely to be affected by the undermentioned events, observations and proposals.

Dr. Hennessy's name removed from the Register.—In May 1945, the G.M.C. erased from its register the name of Dr. Arthur Henry Hennessy, a general practitioner of Sanderstead, for criminally assaulting on 26th September, 1944, an unnamed woman patient, with the intention of committing adultery with her. The public was not admitted to the long hearing. Dr. Hennessy had no right of appeal before any other tribunal. Such is the power of the G.M.C. in penal matters (Editorial, *B.M.J.*, 1946).

Dr. Hennessy sued his accuser for slander and won his case.—In April 1946, Dr. Hennessy sued in the High Court for slander the woman, Miss Irene Boyanton of Sanderstead. He called evidence to show that since the hearing before the G.M.C. she had alleged to two persons in the neighbourhood that he had made indecent advances to her and criminally assaulted her in his surgery. Some of the evidence had not been given previously before the G.M.C.

Mr. Justice Charles said in his judgment that he utterly disbelieved Miss Boyanton's story of the assault. She had lied. For the slander the doctor was awarded £2,000 damages. The judge offered to communicate with the G.M.C. with a view to reinstating Dr. Hennessy as a gross miscarriage of justice had occurred. The offer was accepted gratefully by Dr. Hennessy's counsel (Editorial, *B.M.J.*, loc. cit.).

Inherent flaws in the power and procedure of the G.M.C.—Since its creation in 1858 the G.M.C. has adopted its own procedure, followed its own methods of obtaining proof, obeyed dictates of natural justice and controlled the medical profession with an efficiency which is the envy of other systems in other countries. Yet there are, it is held to-day, three flaws in its constitution: (1) It does not possess the power to compel a witness to attend. (2) It does not possess the power to compel an attending witness to take the oath. As a result

of the lack of these two powers the evidence the Council obtains is inferior to the one obtained in courts. (3) It does not possess the power to award costs against the unsuccessful party. This is a serious weakness in an organization possessing penal power.

Elsewhere in this journal (p. 488) appear proposals drawn up by medical and dental defence unions of Great Britain for introducing the necessary reform in the power and procedure of the G.M.C.

REFERENCE

EDITORIAL *The Brit. Med. Jour.*, ii, 6th July, 1946, 21.

VENEREAL DISEASES NUMBER

It is proposed to publish a special number, in October next year, on venereal diseases in India. Original and special articles on their diagnosis, prevalence, complications and treatment will be welcome.

Contributions will be received up to July 1947 and placed before a special editorial committee.

It has been established gradually during the last 10 years or so that the venereal diseases do not thrive in India. Serious doubts have been cast on the previous estimates according to which 20 per cent of the population not showing any signs of syphilis consisted of latent cases of the disease. Such a state of things in India is impossible for a variety of reasons (*vide* this journal, vol. 81, 1946, nos. 6-7, p. 253). Contributions running counter to the old estimates need not therefore be held back in diffidence any longer.

Venereal diseases other than syphilis and gonorrhoea, some of them of special tropical interest, are very seldom discussed in the current medical literature in India. Recently they have been commented upon in this journal (vol. 81, 1946, no. 9, p. 365).

Medical News

CONQUEST OF DIPHTHERIA

By JOSEPH KALMER

(Reprinted from Release No. F. 103 offered by the United Kingdom Publicity Services, New Delhi)

IN 1945, 614,329 children in Britain were immunized against diphtheria, an increase of 52,015 over the 1944 figure. Ever since the campaign against this disease started in 1940—it claimed some thousands of victims every year—the number of immunized children has increased to 5,979,284—in round figures 6,000,000. This year, before the greater winter diphtheria incidence sets in, a further 550,000 babies at least are to be immunized.

There were 720 fatal cases of diphtheria in 1945—and 25,223 cases. This is a record low point, taken in comparison with the population figure, never before attained in Britain or in any other country. The authorities aim to bring about the total disappearance of diphtheria, and the Ministry of Health is of the opinion that this can be achieved, if the majority of

children are immunized before their first birthday. But 40 per cent of the children in England and Wales are still unprotected against diphtheria.

No scheme of compulsory immunization exists in Britain, nevertheless, the process is making rapid progress, for the public can see the advantages to be gained through immunization from the campaign undertaken by the Ministry of Health in co-operation with local authorities, doctors, chemists and welfare workers.

When the campaign against diphtheria opened in 1940, the primary aim of the Ministry of Health was to protect Britain against illness breaking out on an epidemic scale during the war.

Glancing at the figures for fatal cases given below, the results achieved can only be described as very impressive :

Year	Recorded cases	Deaths
1935	65,084	3,408
1936	57,795	3,003
1937	61,341	2,898
1938	65,008	2,931
1939	47,343	2,133
1940	46,281	2,480
1941	50,797	2,641
1942	41,404	1,827
1943	34,662	1,371
1944	29,949	934
1945	25,223	720

From these figures it can be seen that, since immunization was started not only have cases of infection, but the death rate too has shown a steady decline. This success was achieved under war conditions.

In sharp contrast to these figures is the devastation wrought during the World War II by diphtheria in European countries whether or not occupied by the Nazis. As far as incomplete statistics allow us to form any picture, it appears that the continent during the war had the greatest diphtheria incidence for the last 50 years.

For instance, in Germany, where there was an average of 78,452 cases before the war, the figure for 1942 was 282,859 recorded cases. Cases of infection, too, showed a strong tendency to rise in other countries, including Holland, Norway and Denmark. Even neutral Sweden, which had only 100 cases in 1939, had to record 10 times that number in 1942.

In England and Wales, the Government aims at immunizing 75 per cent of all children under 15, in order to ensure the further fall in the number of diphtheria cases until epidemics disappear. At the end of 1945, there were, in England and Wales, about 8,876,000 children under 15, and each year between 650,000 and 750,000 births are recorded.

In 1939, the rate of children immunized was 8 per cent, in 1941, 30 per cent and, by 1942 it had already increased to 50 per cent and by 1945 to 58 per cent.

Immunization does not guarantee absolute security against diphtheria, but it affords a very high degree of protection. One has only to look at the statistics quoted to see that the number of deaths and recorded cases of diphtheria are in steady decline, and it can certainly be assumed that, in the course of the next few years, the immunization campaign of Britain's Government should have led to the disappearance of diphtheria.

INOCULATION AND VACCINATION CERTIFICATES

Information has been received by the Public Health Commissioner with the Government of India that periods of validity of inoculation certificates of cholera, typhoid and para-typhoid, and vaccination certificates of smallpox, required of passengers proceeding from Indian ports by sea or air to the Netherlands Indies (or passing through Sourabaya) will now be as follows :—

(i) Certificates of vaccination against smallpox—not less than 14 days and not more than 3 years, unless

the passengers bear evidence of a previous attack of smallpox or show local signs of an early vaccination reaction indicating adequate immunity.

(ii) Certificates of inoculation against cholera—not less than 6 days and not more than 6 months.

(iii) Certificates of inoculation against typhoid and para-typhoid—not more than one year.

This supersedes all previous notifications on the subject.

JOURNAL OF THE HISTORY OF MEDICINE AND ALLIED SCIENCES

In future the new quarterly journal mentioned above will be issued in the United Kingdom and the British Empire by William Heinemann Medical Books Limited (99, Great Russell Street, London, W.C.1), Vol. I, No. 3, will be available during the next few weeks. The English subscription terms are 50s. per annum (or four issues) and 12s. 6d. per single issue.

HASSAN SUHRAWARDY, M.D., LL.D., D.Sc.,
D.P.H., F.R.C.S.I.

On 18th September in Calcutta passed away Dr. Hassan Suhrawardy (known until recently as Sir Hassan Suhrawardy) at the age of 62.

Born at Dacca he received his medical education in Calcutta. Later he paid several visits to Europe and to other countries to acquire further qualifications.

He was a member of the staff of the East Indian Railway and he ultimately became the head of the medical department of that railway. He also held the chair of Public Health at the Calcutta University of which, later, he became the Vice-Chancellor and Dean of the Medical Faculty.

Concurrently or subsequently he served in the Army Reserve rising to the rank of Lieut.-Colonel, commanded Second Battalion, Calcutta University Training Corps, was in the Bengal Legislative Assembly, was a First Class Magistrate and a J.P., was President of the Calcutta Branch of the B.M.A., was President of the Board of Studies in Arabic and Persian, and was Adviser to the Secretary of State for India. This list is not exhaustive of the many services Dr. Suhrawardy rendered to the British Government, his community and his country.

In 1932 he was knighted for an act of bravery when a girl student attempted to shoot the Governor of Bengal in the Senate Hall of the University. This knighthood he renounced recently in obedience to the dictates of a political party.

In the beginning of the World War II, when the grant of a site and funds for a new mosque in London was announced, Dr. Suhrawardy spoke in the B.B.C. broadcast to India. In the place of a speech, which he said, he could not manage due to a cold, he recited part of a verse from Iqbal : *Magreb Ki Wādiyon men goonji azām hamāri* (in the valleys of the west echoed our call to prayer).

Dr. A. C. Ukil, a friend of Dr. Hassan Suhrawardy, writes :—

I had known him for over 35 years. He was well known for his affable manners and genial temperament. I have known him as a house surgeon, I have known him when he attained eminence in later years and I have also known him as a patient. When I saw him during his last illness, he recited to me from *Geeta*, in Sanskrit, to my surprise and expressed sentiments which are in tune with the principle of all religions, although he had joined the Muslim League and had given up his knighthood earlier in obedience to the instructions of that party.

Lieut.-Colonel C. L. Pasricha, Director, School of Tropical Medicine, Calcutta, writes :—

I had the pleasure and privilege of knowing Dr. Hassan Suhrawardy for about 20 years. Professionally and socially he was outstanding. He was an example of a perfectionist—one who took meticulous care of detail.

Public Health Section

INCIDENCE OF INFECTIOUS DISEASES
DURING THE PURI CAR FESTIVAL,
1946

By K. N. MISRA, B.Sc., M.B., D.T.M.
Civil Surgeon, Puri

ONE hundred and twenty-seven cases of cholera, bacillary dysentery and non-specific diarrhoea were admitted to the infectious diseases ward of the Government Headquarters Hospital, Puri, during the Puri car festival period from 13th June to 12th July, 1946 (both days inclusive). These cases were divided into mild, severe and moribund groups according to the condition of the patients at the time of admission. Cases with perceptible pulse at the wrist were grouped as 'mild', those with no pulse at the wrist as 'severe', and those admitted in comatose or gasping condition as 'moribund'.

The following procedures were adopted in treatment: (1) Cases on admission were examined carefully. Intravenous or subcutaneous saline was given as the general condition demanded.

Cases admitted with high degree of acidosis received soda-saline besides sulphaguanidine tablets (0.5 gm. each) powdered, 6 on admission followed by 2 every 6 hours.

(2) Stools of the patients were collected immediately after admission and sent to the clinical laboratory for examination and report. On receipt of the report the cases were divided into bacillary dysentery, cholera or non-specific diarrhoea (in which no definite causative bacteria were found).

Bacillary dysentery cases were treated with M.&B. 693 tablets (0.5 gm. each), 1 tablet four times a day with four doses of alkaline mixture given alternatively.

Cholera cases were treated with sulphaguanidine 2 tablets every 6 hours after an initial dose of 6 till the stools were reduced to 4 or 5 per day after which they were given 1 tablet every 6 hours till the stools were reduced to 1 or 2 per day.

Non-specific diarrhoea cases were given sulphaguanidine 4 tablets 3 times a day and kaolin drink (2 oz. per pint) per day.

(3) *Diet*.—All the patients received no diet till the number of stools was reduced to 4 or 5 per day. Then they were given 'barley water' and later 'dahi and rice' gradually.

(4) The treatments adopted for complications are given below :—

Uraemia

- (i) Dry cupping in the kidney areas.
- (ii) Intravenous glucose 25 per cent 25 c.c. twice daily or more often.
- (iii) Mist. alkaline 1 oz. four times a day.

Edema of lungs

- (i) Atropinæ sulph 1/100 gr. per day.
- (ii) Mist. stimulant expect. 1 oz. t.d.s.
- (iii) Tinct. benzoine inhalation twice daily.
- (iv) Lin. camphor co. to rub over the chest and bandage.

Tympanitis

- (i) Stop food.
- (ii) Pituitrin 1 c.c. intramuscularly.
- (iii) 'Castor oil' or 'flatus' enema.
- (iv) Turpentine stupe over abdomen thrice daily.

Persistent hic-cough

- (i) Atropinæ sulph 1/100 gr. per day.
- (ii) Mustard plaster over the epigastrium for 10 minutes or less.
- (iii) Chloretone 5 grs. and sodium bicarbonate 10 grs. three times a day.
- (iv) Glucose 25 per cent or 25 c.c. i.v.b.d.
- (v) Subcutaneous saline whenever necessary.

Persistent vomiting

- (i) Tr. iodine drops (1 drop in an ounce of distilled water) every hour for 8 hours.
- (ii) Fractional doses of calomel with sodii bicarb for a day.
- (iii) Ice to suck.

The following results were obtained :—

Bacillary dysentery (bacteriologically positive).

		Cure	Death
Mild	10	10 (100%)	nil
Severe	15	14 (93%)	1 (7%)
Moribund	3	1 (33%)	2 (67%)
TOTAL	28	25 (89%)	3 (11%)

Cholera (bacteriologically positive).

		Cure	Death
Mild	3	3 (100%)	nil
Severe	5	5 (100%)	nil
Moribund	3	1 (33%)	2 (67%)
TOTAL	11	9 (82%)	2 (18%)

Out of 11 cases, 5 were inoculated against cholera and the death amongst them was nil. Among the non-inoculated numbering 6, the death was 66 per cent.

Non-specific diarrhoea.

		Cure	Death
Mild	30	30 (100%)	nil
Severe	42	37 (88%)	5 (12%)
Moribund	16	1 (6%)	15 (94%)
TOTAL	88	68 (77%)	20 (23%)

Most of these patients were pilgrims who were generally exhausted by irregular diets and long journeys.

Total number of deaths out of these 127 cases was 25 (about 20 per cent) due to following causes: uræmia 2; heart failure due to extreme asthenia 22; toxæmia due to parotitis after diarrhoea 1.

Current Topics

Artificial Sunlight

(Abstracted from the *Medical Officer*, Vol. 75, 15th June, 1946, p. 230)

The Industrial Health Research Board's Report No. 89: Artificial Sunlight Treatment in Industry, by Dora Colebrook, is a work of exceptional value, for it debunks one of the worst stunts which have disgraced the history of medicine. It is not questioned that ultra-violet light is of benefit in treating and possibly preventing some pathological states. But to hold, or even suggest, that ultra-violet light, apart from what falls naturally on the inhabitants of the earth, had special health-giving properties is unwarranted by anything we know of its physical and biological properties.

Life on the earth is possible because our atmosphere stops most of the short-wave radiations of the sun. What reaches the surface is mostly stopped by the integuments of the earth's inhabitants. The amount of light varies greatly in different zones of the earth and the coverings of the animals vary so that wherever they live they are protected against too much irradiation. So far as man is concerned, he attains the greatest measure of health, the highest activities and the best physical and mental powers where there is least light.

Dr. Colebrook did her work well, particularly, in recognizing the importance of treated controls, for thereby she could show that the alleged psychological effects of light treatment are as mythical as its physical value. Undoubtedly in this country a sunny day has great stimulating value mainly, we suspect because it is a rarity. Those who live in sunny climates find an even greater stimulation in cloudy weather—when they can get it. Whether sun-bathing does anything apart from promoting laziness is open to question. The report shows that irradiation did nothing whatever for factory and office workers, but had an insignificant value in coal-miners of Yorkshire who are largely deprived of what natural sunshine is generally available. Dr. Colebrook's researches also throw some light on the uselessness of vitamin therapy where the natural supply is sufficient. This is not new, for we have much evidence that excess of vitamins does nothing whatever—it is merely discarded.

Many measures for treating and preventing disease, at one time welcomed with a blare of trumpets, have gone into complete oblivion, not because they were of no value, but because their benefits were exaggerated and they were applied without discretion in defiance of what was proved. Light treatment and vitamin therapy have proved values and as such should remain in our armamentarium, but they are not elixirs; their use as such discredits both, brings contempt on our profession and makes us ridiculous.

Chemotherapy in Influenza

(From the *Lancet*, ii, 24th August, 1946, p. 277)

Virus infections, with the possible exceptions of trachoma, lymphogranuloma inguinale, and lymphocytic

chorio-meningitis, do not respond to drugs of the sulphonamide group. The influenza virus is one of those against which no chemotherapeutic agent has yet proved effective. There is ample experimental and clinical evidence that sulphonamides and penicillin do not alter the course of uncomplicated influenza; but there is equally clear evidence that these drugs have a definite place in the treatment of secondary bacterial pulmonary conditions. Disagreement about their clinical value in influenza may have arisen for several reasons. With secondary bacterial pneumonia there is no way of judging the severity of the viral infection; and if death results, this is usually attributed to incapacity of sulphonamides to cure, whereas the lethal factor may have been not bacterial but viral. Moreover, sulphonamides are not always prescribed in sufficient doses. It is by no means rare for manifestations of inflammatory lung disease to persist, after a short course of chemotherapy, into convalescence, yet when a further, and full, course is given, the infection is controlled. Apparent failure of sulphonamides can often be traced to faults of technique in their exhibition.

Detailed investigation into the mechanism of the sulphonamides in combined infections with the influenza virus and bacteria have indicated that the severity of the viral process is unaffected by superimposed bacterial pneumonia. Conversely, sulphonamides exert their antibacterial action even in the presence of a rapidly multiplying influenza virus and of extensive pulmonary exudate. This is probably because the virus, though destroying the ciliated cells of respiratory epithelium and so probably lowering resistance to bacterial invaders, does not interfere with the activity of the phagocytic cells which are important in chemotherapy. There is thus good reason for continuing to treat specifically the bacterial pneumonic complications of influenza. We may hope thereby to lower the risk of death, provided that the viral infection itself is not too severe. The white cell count in conjunction with the clinical picture is sometimes a useful guide to the patients most likely to benefit from chemotherapy: leucopenia suggests that the infection is predominantly viral and not susceptible to this treatment, whereas a leucocytosis favours the chance of a good response.

Soya Bean Again

(Abstracted from the *Lancet*, ii, 17th August, 1946, p. 245)

AYKROYD AND KRISHNAN, well before the late war, showed that addition of soya bean to the diet of mission school-children improved their growth rate not a whit, whereas skim-milk powder improved it remarkably. And now the whole subject has been reinvestigated by a subcommittee of the Nutrition Advisory Committee of the Indian Research Fund Association. Working with young and adult rats and human beings, experiments were made on the biological values of soya bean and other pulses, and the effect of soya bean and other supplements on the growth of rats and of children was tested in the Universities of Dacca and Lahore, the Seth G. S. Medical College, Bombay, and the Nutrition Research Laboratories, Coonoor. The results were concordant and led to the conclusion that 'although soya bean contains more of fat, minerals, vitamins and "available" proteins than other pulses, it has, for some unknown reason, not proved itself superior to other pulses within the range of experiments reported. . . . Taking the results obtained so far into consideration, the subcommittee is of the opinion that as a supplement to typical Indian diets based on cereals, but adequate in quantity, soya bean has no special advantages over common Indian pulses'.

Of course, as the committee says, this is not the last word on the nutritive value of the soya bean; but it seems to be losing a little of its prestige.



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The Choice of Sulphonamides

By F. HAWKING

(From the *Practitioner*, Vol. 156, January 1946, p. 72.
As abstracted in the *Tropical Diseases Bulletin*, Vol. 43,
April 1946, p. 380)

In this short note Hawking includes a table which summarizes clearly the sulphonamides suitable for the treatment of certain diseases. It is a condensation of the information contained in the Medical Research Council War Memorandum on the Medical Use of the Sulphonamides.

Table showing which sulphonamide to use in different conditions

Condition	Sulphonamide
Hæmolytic streptococcal infections (moderately severe)	Sulphanilamide.
Hæmolytic streptococcal infections (severe)	Sulphathiazole, sulphadiazine or sulphamezathine.
Otitis media	" " "
Meningococcal meningitis	" " "
Purulent meningitis	" " "
Pneumonia	" " "
Staphylococcal infections (if penicillin is not available)	" " "
Chancroid	" " "
Lymphogranuloma inguinale	" " "
Peritonitis (for insertion after operation)	" " "
Gonorrhœa (if penicillin is not available)	" " "
Urinary infections	Sulphathiazole or sulphamezathine.
Wounds and burns (local applications)	Sulphathiazole, sulphanilamide or mixture of the two.
Bacillary dysentery	Succinylsulphathiazole, sulphaguanidine or sulphadiazine.
Prophylaxis against meningococcal infections or rheumatic fever.	Sulphadiazine, sulphamezathine or sulphanilamide.

occupation and the more urgent need for immunization against diphtheria. It was also thought that further knowledge of B.C.G. vaccination should be obtained before it was advocated for general use. But these considerations did not prevent the systematic B.C.G. vaccination of all Mantoux-negative members of hospital staffs. During the summer of 1943 x-ray surveys were made of several Danish towns, in some of which B.C.G. vaccination of all tuberculin-negative persons had already been undertaken. In this way material, including controls, was provided. In November 1944, the Danish National Tuberculosis Association suggested to the ministry of health an extension of B.C.G. vaccina-

Epidemic Epididymo-Orchitis in Malta

By R. E. TUNBRIDGE

and

C. J. GAVEY

(Abstracted from the *Lancet*, i, 25th May, 1946, p. 775)

A NON-SPECIFIC epididymo-orchitis developed in epidemic form among service personnel in Malta during the summer of 1943.

The cases were characterized by a short prodromal fever, an apyrexial interval of 6 days, followed by a second, testicular, fever lasting 4 days. This testicular fever was accompanied by unilateral testicular swelling, which subsided considerably during the first week, leaving residual swelling, which usually resolved within a month.

The local physical signs indicated an epididymo-orchitis with greater stress on the epididymis.

Though complete recovery was the rule, the epidemic caused substantial invalidism during the summer. Atrophy of the testis followed in 2 patients, and another showed doubtful atrophy.

The aetiology of the condition—a primary (non-specific) epididymo-orchitis—is discussed. We found insufficient evidence to incriminate either a gonadotropic strain of sandfly fever or undulant fever as the cause of the epidemic.

B.C.G. in Denmark

(From the *Lancet*, i, 25th May, 1946, p. 788)

In Denmark, as in other Scandinavian countries, much attention has been paid to the potentialities of B.C.G. vaccination. A full-scale investigation was impossible in the war years owing to the German

tion, particularly for those between the ages of 15 and 25. A report issued in February 1945 shows that B.C.G. vaccination increased to such an extent between 1940 and 1945 that there is now a prospect of all school-children between the ages of 10 and 14 being vaccinated during the next two years. A standing committee has been appointed to deal with the further development of this measure, and it is noteworthy that its six members include a representative of the Danish general practitioners.

A Critical Analysis of the Value of the Addition of A and B Group-Specific Substances to Group O Blood for Use as Universal Donor Blood

By L. H. TISDALL *et al.*

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 31, April 1946, p. 437)

As little as 25 c.c. of a group B plasma containing a high titre of isoagglutinins caused a hæmolytic reaction when administered to a group A recipient.

A and B group-specific substances will reduce a high isoagglutinin titre to low levels.

Experiments on the administration of plasma with high titres of anti-A agglutinins to group A recipients present definite evidence that the addition of group-specific substances A and B is a safe and reliable method for preparing all group O blood for use as universal donor blood for military purposes.

A and B substances are capable of antibody stimulation even when in combination with the anti-A and anti-B agglutinins of group O blood. This calls for some caution in administering such material to women potentially capable of childbearing.

For use as universal donor blood in civilian hospitals, Rh-negative group O blood, selected for its low natural isoagglutinin titre, is somewhat preferable to random group O blood to which group substances have been added to reduce the isoagglutinin titre.

Centenary of Anæsthesia

(Abstracted from the *British Medical Bulletin*, Vol. 4, No. 2, 1946, p. 81)

THERE are several dates of importance in the early history of anæsthesia, and the centenary of some of these has already been celebrated. The year 1946, however, marks the conclusion of a hundred years of uninterrupted progress, and to accept this year as the centenary of anæsthesia is not to ignore the claims of earlier pioneers who, for one reason or another, did not, as Morton did in 1846, effectively initiate the universal adoption of anæsthesia for surgical operations.

It is remarkable that inhalation anæsthesia, which was developed almost exclusively in America and Britain, has for so long remained virtually an Anglo-American Speciality. In other countries, local and, more recently, intravenous methods have been favoured. However, modern surgical requirements, especially in the fields of plastic and thoracic surgery, have made some forms of inhalation anæsthesia almost obligatory and there would seem to be little doubt that inhalation methods will be considerably extended in countries which have hitherto been content to rely mainly upon other techniques.

The extension of inhalation anæsthesia carries with it the implication that the surgeon can no longer be responsible for the administration of the anæsthetic. If the patient is to receive the full benefit of available techniques of anæsthesia, it is essential that the choice and administration of the anæsthetic should be the responsibility of the specialist anæsthetist. This involves the question of the proper status and responsibilities of the anæsthetist. In recent years this question has been a subject of discussion in Britain and America, and in the latter country the word 'Anesthesiology' has been devised to denote a range of duties which includes much more than the technical details of the administration. This neologism may have its detractors, but it is useful because it emphasizes the contrast between the newer conception of the 'Anesthesiologist' and the older conception of the anæsthetist as a pure technician. Dr. John S. Lundy, of the Mayo Clinic, has recently (*Curr. Res. Anesth.*, 1946, 25, 41) defined anesthesiology as: '... the administration of anæsthetics and associated activities. These activities include the use of blood and blood substitutes and the support of the patient in shock, during anæsthesia and afterward; the use of stimulants in connection with support of the patient's circulation and the stimulation of his breathing and reflex activities of his body'.

There are some peculiarities of the anæsthetist's vocation. In other branches of medical practice, the outcome of therapeutic procedures is often conjectural, and their choice may be founded more upon pious hope or uncritical faith than on reasoned expectation. The task of the anæsthetist, however, is precise and unequivocal, and the techniques that he employs are clearly designed to effect a known result which is an end in itself. Every induction of general anæsthesia is an act of applied pharmacology, and the anæsthetist is performing upon the human subject the equivalent of a physiological demonstration. Nevertheless, although anæsthesia has come so far since the days of Morton, the bold empiric, progress was for many years confined to the perfection of practice and technical methods, and the anæsthetist did not fully exploit his unusual advantages. More recent developments give ground for the belief that there will be an increasing field for collective scientific work by chemists, physiologists, pharmacologists, and anæsthetists, and

even the physicist has a part to play in the solution of special problems.

In this number of *British Medical Bulletin* no attempt has been made to produce an account of the practice of anæsthesia. The contributors deal with experimental and clinical subjects, the common feature of which is relative novelty. As is appropriate on the occasion of such an important centenary a considerable amount of space has been allotted to historical material. Readers who wish to obtain practical information on modern anæsthesia will find their needs admirably served by Dr. C. Langton Hewer's *Recent Advances in Anæsthesia* (5th edition, London, 1944) and *Modern Anæsthetic Practice* (2nd edition, 1946) edited by the late Sir Humphry Rolleston and Professor A. Moncrieff, and other well-known textbooks.

A Neurotropic Virus Isolated from *Aedes* Mosquitoes Caught in the Semliki Forest

By K. C. SMITHBURN *et al.*

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 26, March 1946, p. 189)

1. A FILTRABLE virus, believed to be hitherto unknown, has been isolated from *Aedes* mosquitoes caught in uninhabited forest in western Uganda. It has been provisionally named Bunyamwera virus in respect of the locality in which it was encountered.
2. The agent is pathogenic for white mice and exerts its principal pathogenic effects on the nervous system regardless of the route by which it is introduced.
3. The effects of the virus in rhesus monkeys and rabbits are discussed.
4. The agent elicits the formation of virus-neutralizing antibodies in animals which survive inoculation. The presence of these antibodies may be ascertained by intracerebral or intraperitoneal tests.
5. Bunyamwera virus is immunologically different from the viruses of yellow fever, Bwamba fever, St. Louis and Japanese B. encephalitis, Rift Valley fever, eastern and western equine encephalomyelitis and horse-sickness, from West Nile and Semliki Forest viruses and from another neurotropic virus isolated here but not yet reported.
6. Neutralizing antibody against the virus has been found in a forest monkey, in a human who suffered a recent attack of febrile illness characterized by marked neurological signs and in a number of persons sampled at random.

Powers and Procedure of the General Medical Council

(From the *British Medical Journal*, ii, 6th July, 1946, p. 21)

A memorandum on Proposed Variation of the Powers and Procedure of the General Medical Council has been drawn up by the Medical Defence Union, Ltd., the London and Counties Medical Protection Society, Ltd., and the Medical and Dental Defence Union of Scotland, Ltd.

PROPOSALS FOR REFORM

THE Councils of the three defence bodies are of opinion that the existing powers and procedure of the G.M.C. require strengthening and amendment to bring them into alignment with modern practice in criminal courts and courts-martial regulated by rules of procedure similar to those of the Disciplinary Committee of the Law Society. Having posed certain questions to and received the opinion of counsel, the societies submit the following decisions for the consideration of the G.M.C., believing that their adoption would redound to the benefit of all concerned.

That the General Medical Council be empowered and required to establish two distinct and separate committees to be known as (a) the Penal Cases Committee and (b) the Disciplinary Tribunal. That a

member of the Penal Cases Committee be not eligible to sit as a member of the Disciplinary Tribunal to hear a case that has already been before him as a member of the former committee.

That the Disciplinary Tribunal, sitting with a legal assessor, consist of 7 members drawn from a panel of 12 members elected by and from the G.M.C.; that its quorum consist of 5 members, and that it be vested with the full disciplinary and judicial powers of the G.M.C. That complaints received by the G.M.C. be examined in the first instance by the Penal Cases Committee to determine whether a *prima facie* case exists for reference to the Disciplinary Tribunal for determination.

That the General Medical Council be incompetent to present any case in which a Government Department or a constituent body is the complainant, and that the burden of the presentation of any complaint be undertaken only when the Council is satisfied that justice would be denied in the absence of its intervention. That the initial complaint in all cases, including information laid by a Government Department, be supported by an affidavit or affidavits setting out all material facts. That a copy of the affidavit or affidavits be furnished to the respondent with any request addressed to him to provide a reply and explanation. That the respondent be given not less than four weeks' notice of any inquiry to be held by the Disciplinary Tribunal with discretionary power vesting in the President to extend the time on the receipt of an application to this effect.

That the attendance of witnesses and the production of documents before the Disciplinary Tribunal be enforceable by subpoena. That all evidence before the tribunal be given orally on oath save for good and sufficient reason, except evidence as to character, which may be given in writing. That each party furnish to the other not later than 10 days before the hearing of the case a list of the documents on which they propose to rely. That notice to produce and admit be not permitted.

That the Evidence Act, 1938, be not made applicable to the proceedings of the Disciplinary Tribunal. That the parties be entitled to require the tribunal to subpoena any deponent to an affidavit to give oral evidence. That only those documents which are agreed by the parties and such others as are proved in evidence be placed before the tribunal.

That a summing up by the legal assessor be not required unless it is requested by the Disciplinary Tribunal or one of the parties when in the opinion of that party a point of law is involved. That if and when the legal assessor sums up, he be obliged to do so in the presence of the parties. That the legal assessor be a barrister or a solicitor experienced in the practice of the Courts of Common Law and of not less than 10 years' standing.

That provision be made for a right of appeal to the High Court by the respondent on points of law only. That in the event of an appeal any order for erasure be suspended until after the disposal of the appeal, subject to the appeal being entered within 7 days from the date of the order.

That the Disciplinary Tribunal be empowered (in addition to the present penalty of erasure) to administer other penalties short of erasure—viz, suspension for varying periods or censure of differing degrees. That the tribunal be empowered to award costs against a complainant or respondent and that machinery be established for taxing the costs.

That the General Medical Council be given the power, but not the exclusive power, to conduct prosecutions for infringements of the Medical Act, 1858.

That the words 'professional misconduct' be substituted for the words 'infamous conduct in a professional respect' and used in the same connection.

That the rules of procedure relating to penal inquiries be not subject to the approval of a judicial authority.

That the appropriate provision of the Medical Act be amended to permit of the imposition of a maximum penalty of £500 and the alternative of a term of

imprisonment for persons convicted of falsely holding themselves out to be registered medical practitioners.

That addition be made to the present protected designations appearing in Section 40 of the Medical Act to embrace abbreviation of recognized medical qualifications, the courtesy title of 'Dr.' when associated with the healing art, and any other description in common use that is accepted by the public and the profession as indicating that the user is a registered medical practitioner.

Action of Penicillin, especially on *Treponema Pallidum*

By CHESTER N. FRAZIER, M.D.

and

EDWARD H. FRIEDEN, Ph.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 677)

PENICILLIN differs from common antiseptics in that it is not a general protoplasmic poison and simulates sulphonamides and antibiotic substances in that it inhibits the growth of cells.

The antibacterial activity is most potent on Gram-positive organisms. Colon-typoid, hæmolytic and chromogenic bacilli are insensitive, and tuberculous bacillus and trypanosoma equiperdum are resistant.

The antispirochætal potency depends on some fraction of the partially purified product and not on crystalline penicillin.

The mechanism of action, as originally suspected by Fleming, is not only bacteriostatic but also bactericidal. Bactericidal action is more rapid during the phase of rapid multiplication, early lag phase and logarithmic phase of growth and under conditions permitting rapid growth as evidenced by strong inhibitory effect on oxygen uptakes even in very small concentration of penicillin, i.e. 0.4 to 0.1 unit per c.cm., as against no effect on the rate of oxygen uptake even in large concentration during resting phase of cultural cycle of a sensitive organism. In this respect penicillin differs from sulphonamides in that it is capable of destroying bacteria in the early lag phase of growth before actual cell division whereas the sulphonamide acts only after a number of cell divisions have occurred in its presence. The number of surviving organisms decreased geometrically as the period of contact increased arithmetically until 99 per cent of organisms were killed.

Antibiotics, e.g. penicillin, gliotoxin, aspergillic acid and bromo-aspergillic acid, and chemicals, e.g. arsenic, bismuth and mercurial compounds are both spirochætidal agents. Arsenical compounds act by both direct spirochætidal action and combination with sulphhydryl groups in the spirochætes.

In vitro 0.01 unit per c.cm. of penicillin was actively spirochætidal to Reiter's strain of spirochæte and the rate and degree of action increased up to the level of 0.1 to 0.25 units per c.cm. when 90 per cent of the organisms were made nonviable.

In vivo flagella were more sensitive to penicillin than the body. Penicillin destroyed the reproductive capacity of the spirochæte without inhibiting its function of locomotion. If an effective level of penicillin could be maintained in the tissues further increase in the rigor of individual doses would add little to the efficacy of the treatment. Concentration of 0.01 to 0.04 units of penicillin per c.cm. in the blood serum were associated with rapid disappearance of spirochæte from surface lesions and concentration of 0.078 units of penicillin per c.cm. of serum was well above the minimal effective level for destruction of spirochæte. Blood levels of this height were maintained for a period of 12 hours following a single intramuscular injection of 20,000 units and for 2 hours following an intramuscular injection of 40,000 units. Concentration in the relatively avascular tissue will require much higher level.

Elongation of cells, segmentation of pleomorphism of *C. Welchii*, swollen, puffed up, dumb-bell shaped or irregularly outlined ball-like forms in gonococcus and

appearance of long forms or relative increase in the number of long forms (14 to 22 microns as against 7 to 12 microns) with occasional angulation in the middle are some of the changes in morphology of cultured organisms due to the effect of penicillin. The changes are probably due to continuation of growth without the usual division and separation of cells.

Penicillinase, an enzyme-like substance contained in *E. coli*, inhibits the action of penicillin as para-amino-benzoic acid contained in yeast inhibits the action of sulphonamides. As penicillinase may also be found in some sensitive organisms and may not be found in some resistant organisms there is little to suggest the possibility of competitive enzyme system as a basis for the action of penicillin. Penicillin can also be inactivated by various sulphhydryl compounds, e.g. thio-glycolic acid and cysteine. The inhibition of anti-toxins by sulphhydryl compounds occurs as the result of a chemical reaction involving both the substances and leading to the formation of an inactive reaction product. This does not require the hypothesis that the action of the inhibitor is the restoration of normal equilibrium conditions to an enzyme system involving sulphhydryl compounds which was previously disturbed by the antitoxin.

Adaptation of *Treponema pallidum* in vivo to penicillin may be due to the resistance of the host, native tolerance to a particular strain of the organisms and exposure to subcurative doses.

A. B. R. C.

Penicillin Treatment of the Syphilitic Pregnant Woman

By NORMAN R. INGRAHAM, Jr., M.D.

JOHN H. STOKES, M.D.

HERMAN BEERMAN, M.D.

JOHN W. LENTZ, M.D.

and

VIRGENE S. WAMMOECK, M.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 683)

THE writers' conclusions are based on a study, still in progress, of early syphilis treated with sodium penicillin by intramuscular injection and are subject to modification as additional information is accumulated.

One syphilitic infant occurred among 37 syphilitic pregnancies, treated with penicillin, which reached term. In 27 of these cases the infant was followed for periods greater than two months post-natally and the presumptive evidence that the infant was normal was good. This represented a degree of success equal to, if not greater than, that obtained with the arsenical-bismuth regimens at present widely employed.

Either 1.2 million or 2.4 million Oxford units total dosage seemed satisfactory for the pregnant woman, though the larger dosage was preferred. It was recommended that the dosage be reduced to one-fourth during the first twenty-four hours and to one-half during the second twenty-four hours to reduce the possibility of threatened abortion from therapeutic shock and that the duration of treatment be prolonged to eight or nine days.

The serologic response to penicillin treatment of the pregnant woman was apparently considerably slower than the average for early acquired syphilis in the adult. It was not necessary, on the other hand, that the mother be seronegative at the time of confinement in order for the infant to be normal.

As a result of the writers' continued use of penicillin in the treatment of the pregnant woman with early syphilis, the writers were confident that this drug represented a distinct advantage in that it was a convenient, safe and effective mode of therapy.

It was demonstrated through laboratory evidence that penicillin will pass from the maternal to the fetal blood stream at term. There was some indirect clinical evidence in the present study to indicate that penicillin

might traverse the placental barrier earlier in the pregnancy in that nine of the women in the present series were treated after the thirty-second week of pregnancy with uniformly good results when the possibility of infection of the foetus would be presumably high.

Since the foetus may be infected anytime after the sixteenth week, the permeability of the placenta to penicillin from the fourth to the ninth lunar month is a critical issue in the prevention of congenital syphilis by a single course of the drug during pregnancy.

A. B. R. C.

Penicillin Treatment of the Syphilitic Infant

By NORMAN R. INGRAHAM, Jr., M.D.

JOHN H. STOKES, M.D.

HERMAN BEERMAN, M.D.

JOHN W. LENTZ, M.D.

PAUL GYORGY, M.D.

and

ELIZABETH K. ROSE, M.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 694)

THE writers treated with penicillin 26 infants with early congenital syphilis. Of the infants which had been followed for periods longer than 6 months after treatment 10 (71 per cent) remained clinically normal and were seronegative, 4 were clinically normal but remained seropositive. This percentage success does not approach that which is being obtained in early acquired syphilis in the adult.

The range of total dosage employed for infants treated in this series had been from 11,000 Oxford units per pound to 74,000 Oxford units per pound of body-weight given over a period of from seven to fifteen days. The larger total doses with the longer periods of treatment gave the better results.

A. B. R. C.

Penicillin in Prevention of Prenatal Syphilis

By MARY STEWART GOODWIN, M.D.

and

JOSEPH EARLE MOORE, M.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 688)

FIFTY-SEVEN pregnant women with early syphilis at different periods of gestation (less than 16th week to 32nd week) were treated with penicillin in two university clinics. Sixty infants were born to these women, all of whom were born alive; only one developed clinical or laboratory evidence of congenital syphilis. In this one case, syphilis in the child might possibly have been prevented. The remaining 59 infants were all apparently normal, and 42 of these were followed for a long enough time after birth to make practically certain of the diagnosis of 'no syphilis'.

The total dose of penicillin should be not less than 2.4 million units administered intramuscularly in aqueous or saline solution at intervals of not less than two nor more than three hours night and day.

The total duration of treatment should be not less than seven and one-half days.

Retreatment with penicillin should be given during pregnancy to the mother if (a) there is evidence of clinical or serologic relapse or (b) the original maternal serologic titre does not significantly decline within three months after treatment.

Pending further information, a pregnant syphilitic woman previously treated with penicillin, and whether

or not this earlier treatment was apparently successful as to the mother's infection, should be retreated with penicillin in each succeeding pregnancy.

These results in the prevention of prenatal syphilis were superior to any heretofore attainable with any method of treatment.

There was no satisfactory evidence that penicillin was directly or indirectly responsible for abortion from therapeutic shock or direct penicillin action.

Contrary to the observation of earlier workers pregnancy did not seem to exert any effect in showing up serologic response, patients having reverted towards negative at the same rate as non-pregnant females, or males.

It is recommended that in syphilitic pregnant women penicillin be used routinely for the prevention of prenatal syphilis, other methods of treatment being abandoned.

A. B. R. C.

Treatment of Early Syphilis with Penicillin

By ARTHUR G. SCHOCH, M.D.

and

LEE J. ALEXANDER, M.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 696)

FROM personal observation of over 900 adult patients with early syphilis the writers stated that penicillin properly administered will cure the majority of patients with primary and secondary syphilis. The following treatment schedule and remarks are made:—

1. The minimum dosage should be at least 2.4 million units of penicillin; the total time required should be a minimum of seven and one-half days; the interval between individual intramuscular injections should be a maximum of three hours, day and night.

2. In addition to penicillin treatment the patients should receive either oxophenarsine hydrochloride intravenously, 40 mg. daily for 8 doses, or five injections, 0.2 gm. each, of bismuth salicylate in oil on alternate days, or both. The writers themselves prefer the addition of bismuth alone to the penicillin treatment schedule in order to obviate completely the possibility of arsenic reactions inevitable in a large series of cases when oxophenarsine hydrochloride is used even in small amounts.

3. A regular and thorough follow-up of all treated patients for a minimum of five years is essential to proper management. The follow-up must include adequate quantitative serologic determinations and adequate spinal fluid examinations.

4. The management of the occasional penicillin failure should be individualized and expertly planned.

5. We strongly urge that intimate contacts of the patients be treated coincidentally with the treatment of the patient to avoid reinfection.

A. B. R. C.

Penicillin in the Treatment of Neurosyphilis

By PAUL A. O'LEARY, M.D.

LOUIS A. BRUNSTING, M.D.

and

ORVILLE OCKULY, M.D.

(Abstracted from the *Journal of the American Medical Association*, 16th March, 1946, p. 698)

THE preliminary impressions gained in the past two years by treating 100 patients who had various types of neurosyphilis with different methods in which penicillin was employed are summarized:—

1. The outstanding result common to most of the patients in this series following the use of penicillin was a return of the cell count, protein and gold curve to within normal limits in the studies of the cerebrospinal fluid with reduction of the strength of the

complement fixation and titre reaction of the blood.

2. The outstanding clinical effects as noted among patients who had objective and subjective signs of neurosyphilis were a gain of weight and a reduction of severity and frequency of the pains in the legs. The early symptoms of dementia paralytica were not influenced.

3. The patients who had meningeal neurosyphilis were most responsive both clinically and serologically, while patients who had the parenchymatous forms of the disease were helped only slightly if at all.

4. The outstanding serologic results noted were among the patients who had asymptomatic neurosyphilis and who received penicillin intravenously in doses approximating 1,200,000 units in a week, in association with either three spinal drainages or intraspinal treatments (Swift-Ellis type).

5. Penicillin given in combination with fever therapy, either malaria or by means of the fever machine, did not improve the clinical results noted from fever treatment alone.

6. The administration of penicillin by the intravenous, intramuscular or intraspinal route, alone or in combination with fever therapy, both malarial and by machine, leads the writers to believe that penicillin alone is not capable of controlling the parenchymatous forms of neurosyphilis. However, in cases of the meningeal forms of the disease and in those in which there was a high degree of pleocytosis in association with asymptomatic neurosyphilis, the results thus far are encouraging.

7. In occasional cases of neurosyphilis penicillin therapy produces clinical and serologic results that are outstanding. However, these favourable results are noted in only a few cases and often appear when least expected. It is not possible at this time to account for such great therapeutic discrepancies.

A. B. R. C.

The Present Status of Varicose Vein Sclerosing Agents

By I. H. PRATT, M.R.C.S., L.R.C.P.

and

T. D. WHITTET, Ph.C., D.B.A.

(Abstracted from the *Pharmaceutical Journal*, 27th April, 1946, p. 272)

VARICOSE veins occur most commonly in the legs and more frequently in women than in men. In the anal canal they are called hæmorrhoids. They are characterized by a dilatation and elongation of the superficial veins due positively to the damage of the valves causing incompetence by a previous infection. The result is increase of blood pressure in the veins which become long and tortuous.

The indication for injection treatment is the potency of the valves at the junction of superficial and deep veins which is determined by the use of Trendelenburg test. Otherwise operation is indicated. The sclerosing agents produce their effect by their action on the vein wall and to secure best result the vein should be emptied before actual injection is begun.

The following varieties of substances have been used: *Sodium morrhuate*.—It is a sensitizing agent and so may cause anaphylaxis. The formula contains 5 per cent of sodium morrhuate with 1 per cent of ethyl alcohol and 0.1 per cent of chlorocresol. Commercial preparations are:—Episol (The Crookes Laboratories), sodium morrhuate with 20 per cent of sodium chloride; sterules of sodium morrhuate (Martindale); varicane [Pharmaceutical Specialities (May and Baker), Ltd.]; sodium morrhuate, 5 and 10 per cent.

Quinine and urethane.—Patient may have an idiosyncrasy to quinine. Commercial preparations are:—Chinethan (Richter); sterules of quinine and urethane (Martindale); varixon (Evans Medical Products).

Lithocaine.—It consists of procaine hydrochloride 1.0 gm., lithium salicylate 30.0 gm., chlorocresol 0.2 gm., b.

and distilled water to 100.0 mls. It is best for treatment of large veins seated deeper in the tissues. The combined injections of lithocaine and quinine and urethane has proved very satisfactory.

Monoethanolamine oleate.—The preparation contains 5 per cent of the substance containing 25 per cent of glycerine or 2 per cent of benzyl alcohol. It is most safe and commonly used and is suitable for small and superficial veins. Commercial preparations are :—Ethamolin (Glaxo Laboratories, Ltd.), aqueous solution of ethanolamine oleate (5 per cent) with benzyl alcohol (2 per cent) in 2-mil. ampoules and 15- and 30-mil. bottles. E.O.B.A. sclerosant (Wyley's, Ltd.), monolate (Abbott Laboratories), neovaricane [Pharmaceutical Specialities (May and Baker), Ltd.], thanomin (Burroughs Wellcome and Co.), varistab (Boots Pure Drug Co.), a 5 per cent solution of ethanolamine oleate with 25 per cent of glycerine, and moramin (Allen and Hanburys).

Dextrose.—There is a possibility of pulmonary embolism occurring. Commercial preparations are :—Cabiven (Coates and Cooper), a 66 per cent solution of dextrose, issued in ampoules of 5 and 10 mls.

Sodium chloride.—Twenty per cent of solution was used but it has gone out of favour. Commercial preparation is varicophytin (Napp).

Phenol.—2 to 4 minims of undiluted liquefied phenol was used. The injection is practically painless but more toxic than sodium morrhuate and monoethanolamine oleate.

Sodium salicylate.—Because of many disadvantages it has almost entirely passed into disuse. Commercial preparations are :—Sclerovaine (Bengue), ampoules of sodium salicylate solution, and sterules of sodium salicylate (Martindale), which contains 15 grains in 320 minims (1 gramme in 20 mls.).

A. B. R. C.

Rapid Death following Injection of Antitetanic Serum

By ERIC GARDNER, M.B. (Camb.)

(Abstracted from the *Lancet*, 11th May, 1946, p. 689)

THE writer reports a case of injury in left index finger died just after one hour of injection of antitetanic serum into the pectoral muscle with proper precaution to prevent anaphylactic shock. Symptoms before death were : vomiting, increasing respiratory difficulty and cyanosis. Post-mortem findings showed œdema and minute hæmorrhages in all the organs and no reaction at the site of injection or sign of accumulation of antiserum there. From these observations and the rapid onset of symptoms it is probable that the point of the needle had entered a vein into which the injection was made.

A. B. R. C.

Death after Serum

(Abstracted from the *Lancet*, 11th May, 1946, p. 694)

THE death following the administration of antitetanic serum reported by Dr. Eric Gardner on this page should serve as a warning to all who use serum of any kind in prophylaxis or treatment. Fortunately such accidents are far from common. Park in 1928 estimated that the incidence of alarming symptoms is 1 in 20,000, and of fatalities 1 in 50,000. Refined serum has since reduced these accidents to an even lower level.

The pathogenesis of fatalities from such injections is not clear. The aerated lungs, congested veins, and sub-endothelial hæmorrhages all suggest an analogy with fatal anaphylaxis as seen in the guinea-pig. On the other hand, in most of the fatal cases reported in man, there has been no history of any previous injection of serum that might have acted as the sensitizing dose which appears to be essential for the production of anaphylactic phenomena in animals. But in both

man and animal these related conditions are dramatically cured by adrenaline. On the value of preliminary testing for sensitivity to the serum there is a diversity of opinion; certainly little is lost by caution in the rate of administration, but accidents have occurred even after testing for skin sensitivity and injecting in small divided doses. Probably the warning to which most attention should be paid is a history of asthma or of an 'allergic diathesis'. Observance of the following rules would help to prevent similar fatalities : (1) The injection of serum or bacterial toxoid must be made by the doctor or at any rate in his presence. (2) Whenever possible refined serum only should be used; the smaller bulk of this new product is an added advantage. (3) A sense of security should not be harboured on the strength of there being no history of previous injections of serum; and a history of asthma should be regarded as a warning of serious danger. (4) A syringe containing 1 in 1,000 adrenaline should always be at hand.

The Anti-O Agglutinin in Human Blood, with the Report of a Case of its Occurrence

By NOEL R. HENRY, B.Sc.

(Abstracted from the *Medical Journal of Australia*, 23rd March, 1946, p. 395)

A CASE is reported of a patient whose serum contained an anti-O agglutinin of unusual strength. This particular serum was of sufficient potency to yield satisfactory experimental evidence in support of Wiener's theory that if anti-O serum reacted with those properties determined by genes O and A₂, but not with those determined by A₁ or B, then the only blood which would fail to react would be that of genotype A₁B, that of genotype A₁A₂, and that of genotype BB if the serum were of sufficient potency. Its place in the ABO blood group scheme is analogous to the place of anti-Hr serum in Rh blood types. It cannot be definitely determined whether the anti-O agglutinin in the present case is a natural or an immune agglutinin. The relatively high titre of the agglutinin and the fact that it is active at 37°C. are points in favour of its immune nature, but obviously are not conclusive evidences. On the other hand, a sample of serum withdrawn twelve months after parturition approximately the same titre as previous specimens; this is evidence against this antibody's being the result of immunization, since the titre usually decreases when the immunizing stimulus is withdrawn.

Although these cases are rare, they serve to prove that the 'universal' donor does not exist. The usual objections to the use of the universal donor are on the grounds of high iso-agglutinin titres, and it is not universally agreed that the donor's serum can significantly affect the recipient's cells. It is, however, obvious that here the so-called universal donor's cells would be attacked by the patient's serum; so we have a major incompatibility, and a transfusion from a 'universal' donor would probably result in a severe, if not fatal, hæmolytic reaction.

A. B. R. C.

Some Observations Concerning the Use of Hypnosis as a Substitute for Anæsthesia

By R. L. H. SAMPIMON, M.D. (Leyden)
and

M. F. A. WOODRUFF, M.D., M.S. (Melbourne)
(Abstracted from the *Medical Journal of Australia*, 23rd March, 1946, p. 393)

AN account is given of some 29 cases illustrating the use of hypnosis as a substitute for anæsthesia.

The use of hypnosis in these cases was necessitated by rather unusual circumstances, which one may

reasonably hope never to encounter again; but the method was found to possess certain advantages which may justify its use in selected cases in ordinary surgical practice. The advantages referred to are as follows: (i) Nervousness of the patient is entirely eliminated. (ii) Full co-operation of the patient can be secured. (iii) Post-operative pain can be reduced to a minimum, and even in many cases prevented altogether. (iv) The usual complications of other forms of anaesthesia, including post-operative vomiting, do not occur. (v) It appears that in dental cases in which hypnosis is used there may be less hæmorrhage and more rapid healing of the wound than normally occur when other methods are used. (vi) The method may be used in certain cases in which ordinary anaesthetics are contra-indicated or cannot easily be employed, for instance, for patients requiring dental extraction in whom pronounced trismus renders the use of local anaesthetics difficult, and when for some reason or other general anaesthesia is contra-indicated.

The method appears to be safe and reliable, and in particular, once a satisfactory state of hypnosis is induced, the possibility of the patient's waking prematurely during the operation is remote. There is, of course, the risk that by the abolition of post-operative pain complications which supervene may pass unrecognized; but once this possibility is realized the danger is thereby reduced to a minimum.

The present investigation unfortunately (or fortunately) did not go very far; but the results obtained at least indicate some of the possible surgical applications of hypnosis, and suggest that further work done along similar lines might lead to results of considerable value. Such work, if it is to be successful, must be undertaken by a surgeon and a psychiatrist working in collaboration.

A. B. R. C.

Therapeutic Action of Different Penicillins on *Spirochaeta recurrentis* Infections in Mice

By J. WILLIAMSON, B.Sc. (Aberd.)

and

E. M. LOURIE, M.B. (Lond.)

(Abstracted from the *British Medical Journal*, 1st June, 1946, p. 828)

Of the various identified forms of penicillin, that known as penicillin II in Great Britain (i.e. penicillin G in U.S.A.) appears in much greater proportion than any of the others, in batches ordinarily prepared for therapeutic use. Reports of other workers have suggested that crystalline samples of this form of penicillin may be less effective against syphilis than partially purified preparations, such as are normally issued for parenteral injection in clinical practice. If this be the case, then the status of penicillin in the treatment of syphilis stands in danger of deteriorating as production methods improve, with consequent release of batches of a higher and higher grade of purity. However, in so far as trials against *Spirochaeta recurrentis* infections in mice may be an index to the situation, the present experiments do not reveal any superiority of partially purified preparations over crystalline penicillin II.

Penicillin III (penicillin X of U.S.A.) is stated to be significantly more active than penicillin II, or than ordinary partially purified preparations of penicillin, against certain strains of streptococcus, pneumococcus, meningococcus, and gonococcus *in vitro*. It is also believed to have given better results than these other forms of penicillin in the treatment of gonorrhœa. The present experiments show, however, that it is substantially less effective than the other forms in the treatment of *Spirochaeta recurrentis* infections in mice.

A. B. R. C.

Duration of Penicillin in the Blood after Single Injection

By R. M. DOWDESWELL, M.D. (Cantab.)

(Abstracted from the *East African Medical Journal*, Vol. 23, May 1946, p. 139)

THE following conclusions could be drawn from the experiments done:—

1. Penicillin given with gelatin or blood was retained for longer than when given in water.
2. Exposure of the patient to the sun or to a relatively high temperature, led to more rapid disappearance of the drug than when he was exposed to cool temperature conditions.
3. Penicillin given in gelatin or with blood had a similar rate of dispersal.
4. When 100,000 units were given under fairly cool conditions, penicillin might be detected in the blood for more than 7 hours; when 150,000 units were given, it might be detected for more than 9 hours.
5. There was evidence that a single subcutaneous injection of 150,000 units of penicillin with gelatin or with blood would cure early acute gonorrhœa, provided that the patient was kept in a temperature below 75°F., with good ventilation.

A. B. R. C.

Reviews

ACUTE INJURIES OF THE HEAD: THEIR DIAGNOSIS, TREATMENT, COMPLICATIONS AND SEQUELS.—By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.). 1945. E. and S. Livingstone, Limited, Edinburgh. Pp. xvi plus 224, with 201 illustrations, 12 in full colour. Price, 30s.; postage, 7d. (home)

THE second edition of this work (first edition 1942) is sufficient testimony of its usefulness. Appearing as it did at a most opportune time in the early part of the last war it has served us surgeons well.

Written clearly in good simple English the book presents a balanced continuous picture of the acute head injury and all its phases with such emphasis upon first principles that both general practitioner and practising surgeon will draw great profit and closer unity of action in their care of the afflicted from its study.

There are thirteen chapters covering:—

- Mechanisms of injuries of the head.
- Pathology.
- Diagnosis of closed injuries of the head.
- Treatment of closed injuries of the head and surgical technique.
- Fractures of the skull.
- Open or compound wounds of the head.
- Traumatic osteomyelitis.
- The results of injury to special parts of the brain and skull.
- The sequels of injuries of the head.
- Rehabilitation.
- Post-traumatic epilepsy.
- The final results of head injuries.
- The mechanism of birth injuries.

Those on pathology, diagnosis of closed injuries and their treatment are particularly useful. Each chapter however is balanced and self-contained.

The standard of writing is even throughout and the reader's interest sustained in a most pleasing manner. The subject is covered completely.

Head injury centres in this country are as yet non-existent, and organized care of these cases cannot be undertaken in the general surgical wards with anything like the necessary efficiency and effectiveness required to produce results. The results seen in our wards compared with the results detailed by Rowbothan should be a stimulus to us.

There are a few typographical errors such as '180 mm. protein' instead of '180 mg. protein' on page 165 but these are of little moment.

The book is one of Livingstone's best productions. The combination of MacMillan and Rowbothan has resulted in a book which has come to stay as a classic text on acute head injuries.

A. T. A.

INJURIES OF THE KNEE JOINT.—By I. S. SMILLIE, O.B.E., M.B., F.R.C.S.E., F.R.F.P.S. 1946. E. and S. Livingstone, Limited, Edinburgh. Pp. xi plus 320, with 350 figures, some in colour. Price, 36s.

THIS is an eminently practical book, designed to give the results of the author's personal experience with knee joint injuries. It is based on his record of over 5,000 cases seen in the short five years of war at a specially equipped centre in Scotland. As the author remarks: 'A life's work, compressed into the space of five years'. It is a tribute to his organization and industry that he should be able to bring out and publish so clear an analysis of his work only a year after cessation of hostilities.

The book provides an up-to-date survey of the present position of diagnosis and management of injuries to the knee set against the background of the author's personal work. Those of us with anything like comparable personal experience during the war years may disagree with some of the detail. Careful thought shows that criticism is not called for on these points since they mostly resolve themselves into either personal fads or just another way of reaching the same result.

The information contained is clearly set out and illustrated. The book provides the general surgeon with a comprehensive and authoritative guide to the subject. Insistence upon such points as the surgeon being responsible for the application of the compression bandage after operation is good to see. The main difficulties in technique encountered by beginners are dealt with; incidentally many surgeons remain beginners where meniscectomy is concerned. Girdlestone's timely warning on the misuse of weight-and-pulley traction and the author's comments—'Prolonged powerful traction is often prolonged merely because it is powerful, . . .', 'Traction should not be expected to reduce the fracture but merely to maintain the accurate reduction secured by the surgeon'—are well placed in the chapter on the stiff knee. How many stiff knees are due to this type of error in thought and technique the general surgeon and medical officer do not seem to realize sufficiently.

The very short reference to Active Exercise as the key to knee joint recovery on the second page of the book could with advantage have received more attention. The reviewer believes that it is not sufficiently realized that active neuromuscular canalization early in treatment is the royal road to success and no amount of massage and other aids can ever replace it. Emphasis could be more marked throughout the book on this point in after treatment; the point cannot be overstressed.

The book should be read by all medical officers dealing with factory or mine workers, the armed forces, mechanics or athletes. The chapters on the Quadriceps, Traumatic Synovitis and Hæmarthrosis, Clinical Features of Internal Derangements, Injuries to Ligaments and the Stiff Knee deal with subjects of such importance that every general practitioner and student of medicine should read them carefully.

Smillie and MacMillan are to be complimented on their production.

A. T. A.

PENICILLIN IN GENERAL PRACTICE.—By J. L. Hamilton-Paterson, M.D. Staples Press Limited. John Bale Medical Publications Limited, London. Pp. 95. Illustrated. Price, 5s.

THIS little book has gathered for the benefit of the practitioner all information available from the current literature up to May 1946 on the use of penicillin.

Indications for the use of the antibiotic, its dosage, its many preparations, methods of its administration and special apparatus when necessary are given in detail. Utility of periodic high levels of its concentration in the blood, as opposed to a medium sustained level, has been indicated. Need for its contact with the micro-organism involving special methods of administration is emphasized.

The resistance due to a previous inadequate dose, it is stated, can be easily overcome by a subsequent higher dose.

Toxicity, due mainly to impurities, is stated to exist and to be responsible for fever, pain, cedema, a condition resembling serum sickness, erythema and epididymitis.

In a rather elaborate account of a small topic repetitions are obvious (e.g. figure 1 appears again as figure 4 and mega unit is defined on pages 11 and 45).

Only two printers' errors attract attention: (1) Page 45, last para, 2nd line, 'water freshly sterilized for boiling' should be 'by boiling'; (2) page 83, para 2, line 8, 'b. proteus' should be 'B. proteus'.

An admirable publication.

S. D. S. G.

PRACTICAL POINTS IN PENICILLIN TREATMENT.—By G. E. Beaumont, D.M. (Oxon.), F.R.C.P. (Lond.), and K. N. V. Palmer, M.B. (Cantab.), M.R.C.P. (Lond.). J. and A. Churchill Limited, London. Pp. 16. Price, 1s. 6d.

THIS brochure is issued for the benefit of doctors who have not had the opportunity of studying the administration of penicillin in hospital. Although not comprehensive it gives useful information. A difference of opinion may exist on the treatment of superficial eye infections, namely, that, as tears remove the antibiotic very rapidly, for the first half hour drops must be instilled every few minutes (they have been instilled at intervals of one minute). In the complications of penicillin treatment epididymitis (mentioned by some authors and an important item in the treatment of gonorrhœa) has been omitted.

S. D. S. G.

THE CAUSATION OF APPENDICITIS.—By A. Rendle Short, M.D., F.R.C.S. 1946. John Wright and Sons Limited, Bristol. Pp. 79. Price, 10s.

THIS provoking little book is a reconsideration in the light of recent happenings of the author's thesis that a cellulose lack in the diet of the European is responsible for an apparent increase in the number of cases of appendicitis. Rendle Short's original article appeared in the *British Journal of Surgery*, 1920-21, vol. 8, p. 171, and the present booklet with a few additions is mainly a reprint of this.

Many interesting statements are made, such as these two: . . . the great rise (in incidence) took place between 1895, when it was just beginning, and 1905; that since 1905 it has been fairly steady; that there was no drop, but rather an increase, during the years of privation towards the end of the war of 1914-18' (p. 2).

'The food privations of 1917-18 caused a lowering of the death rate from appendicitis amongst the older women, but males and younger women were not affected. During 1940 there was a fall in the death rate in men and women, which became very pronounced from 1941-44 inclusive' (p. 76).

Now these statements although very interesting can hardly be set alongside statements of variation in diet occurring between 1870 and 1944 in the relation of cause and effect without very much more proof than is forthcoming in this book.

The argument that between 1895 and 1905 an increase of appendicitis did occur because the number of cases of 'Perityphlitis' and 'Iliac Phlegmon' noted before that period was very much smaller than the number of cases of 'appendicitis' noted after Fitz's monograph appeared in 1886, is hardly valid. The known effect of the publication was to set the profession on the trail of the appendix, as is shown by the increase in operative treatment when doctors became more familiar with the clinical condition.

The book is full of curious assumptions, and conclusions drawn from inadequate data or even single statements, e.g. the reference on page 25 to vegetarians and appendicitis.

The chapter on National Distribution is a series of short statements under the name of each country. Judging by that under India, the others may at most be little more accurate. The conclusions drawn at the end of the chapter are not justifiable on the evidence adduced. The irritating statement that 'Natives of Asia, Africa and Polynesia seldom suffer, unless they take to *European diet*', appears in several places. It is sweeping and misleading. Firstly, there are no accurate statistics as the author admits (p. 73); secondly, he bases his evidence for India upon the vague (and inaccurate) statements of four individual observers without any mention of their special circumstances or any assessment of the validity of their statements; thirdly, what is a '*European diet*'? In Europe alone the author tells us under his brief consideration of individual nations that each has its own dietary habits. A review of these shows how varied they are. In India very few Indians eat their food prepared in the English way; amongst the poorer 'Europeans' the diet is definitely that of the people of the country and mainly vegetarian. In the Indian Army and amongst civilians, I have seen and operated upon hundreds of cases of acute appendicitis where there was no question of '*European diet*', if by that Rendle Short means the Englishman's diet. Many of my cases were certainly vegetarians.

Nowhere is consideration given in the case of the more primitive countries to the fact that these peoples do not seek doctors in sickness. To them all cures come from magic and Western Medicine is only another form of magic. In pain they retire to their homes, do the things prescribed by their particular beliefs and through rest largely recover. These very countries are just those from which statistics of any sort are impossible.

Gradually the surgeons in these countries are seeing more cases of appendicitis, not because of the spread of any '*European habit of diet*' but because of spread of the news that some cases are cured by Western Medicine. We see many late cases. As the author rightly points out the *death rate* is probably lower where the population eats sparingly and works hard; again this represents the conditions in primitive countries.

Little or no reference is made to the simple facts that the appendix is a *cul de sac* containing a liberal supply of lymphoid tissue which increases in amount up to 18 years of age and then gradually disappears up to 50 or 60 years of age; that it lies at the bottom of the 'caecal pool' of faecal matter; that we still know very little about the reasons for the choice of site for implantation and commencement of disease by bacteria, etc. Wangersteen's work on intraluminal pressure and that of many others is not mentioned.

The book is unsatisfying and the thesis is hardly upheld.

A. T. A.

GYNAECOLOGICAL ENDOCRINOLOGY FOR THE PRACTITIONER.—By P. M. F. Bishop, D.M. (Oxon.). 1946. E. and S. Livingstone, Limited, Edinburgh. Pp. viii plus 124. Illustrated. Price, 7s. 6d. Postage, 3d. (home)

This concise little handbook of Gynaecological Endocrinology for the practitioner can be thoroughly

recommended for the general practitioner and final year student.

Endocrine treatment of women has become a very important part of general practice and a small book such as this one by Dr. Bishop is now long overdue. In it he has briefly, logically and simply described the endocrine control of the menstrual cycle, the sex hormones both natural and synthetic and their dosage and modes of administration. There is a chapter each discussing and advising endocrine treatment for amenorrhoea, excessive bleeding, dysmenorrhoea, the menopause and infertility and the endocrinology of pregnancy and hormone treatment of its complications is advised. Pregnancy tests are described in some detail and there is a final chapter briefly discussing the value and practicability of hormone assays. All this is given in ten short chapters in 81 pages. An appendix provides a complete list of the better-known commercial preparations of sex hormones and gives dosage, packing, modes of administration and the British price. This appendix is very useful.

It is really to be hoped that this excellent book will be bought, read and constantly referred to by practitioners and that it will replace the pamphlets, booklets, and leaflets on endocrine treatment so widely distributed by the commercial drug firms. Those, I am afraid, so often form the basis of the practitioners' knowledge of endocrinology and may be responsible for the most colossal and sometimes dangerous blunders in endocrine treatment.

The only criticism to be offered is that the dangers of incorrect or uncontrolled hormone treatment are not sufficiently stressed. Prolonged overdosage with synthetic oestrogens may be in susceptible subjects, carcinogenic. Incorrect treatment with gonadotropic hormones may, by the formation of antihormones, preclude correct treatment later with these 'tools with which, in the future, we shall mend the disordered menstrual cycle'. These, and the fact that laryngeal changes once induced by the male hormone—given perhaps for puberty bleeding—are irreversible should be very strongly emphasized. A husky voice in a female is not really attractive.

G. B. W. F.

COMPLEMENT FIXATION FOR CLINICAL PURPOSES.—By S. D. S. Greval, B.Sc. (Ph.), M.D., Ch.B., D.P.H. (L'pool), Lieut.-Col., I.M.S. 1946. U. N. Dhar & Sons, Ltd., Calcutta. Pp. 95. Illustrated. Price, Rs. 7-8

COLONEL GREVAL's name is well known for his work on the Wassermann reaction and his many writings on the subject. In this booklet he brings together the results of his previous work and of others and presents an excellent account of the technique of the complement fixation tests. The author points out in the preface that 'titrated positive controls are the only means of determining the comparative intensity of the reaction and fixability of the complement used, on different days'. Details are given for the titration of various reagents used in complement fixation tests. As long as the reagents of this test cannot be replaced by known chemical substances their titration is a matter of great importance. The directions for the actual performance of the tests for various diseases such as syphilis, kala-azar, hydatid disease, gonorrhoea, are given in detail. The author's suggestion that the reaction should be renamed *Lecithin complement fixation (L.C.F.)* is worthy of consideration and adoption, but as we are all weighed down by the 'dead hand of tradition, it will be long before this name comes into general use. The book also contains some useful information regarding interpretation of tests, provocative procedure, false positive reactions, etc. It is worthy of note that the author is against the use of provocative injection which is so popular among clinicians. The decreasing use of this method of emphasizing the reaction is due to several causes of which the most important is the non-specific rise of syphilitic antibody or reagin. Stress has been laid on

the importance of repeating the test in certain cases. There are a few minor errors of figures which do not appear to have been incorporated in the Errata, for example on page 3, 0009/51 c.c. should have been 6000/51 c.c. The book, which is well printed and well bound, is a useful guide for laboratory workers. Its price (Rs. 7-8-0) is justified by the high cost of production at the present time.

A. N. G.

AIDS TO DERMATOLOGY.—By Robert M. B. Mackenna, M.A., M.D., B.Ch. (Camb.), F.R.C.P. (Lond.). Third Edition. 1946. Baillière, Tindall and Cox, London. Pp. viii plus 309. Price, 6s.

This is a nice little book of the aid series suitable alike to the students and for the general practitioners as a ready reminder. It contains information helpful also for the post-graduate study. By the omission of the chapters on syphilis the space has been well utilized on skin diseases.

The book has been brought up to date and the more common diseases have been dealt with satisfactorily.

The publishers deserve congratulation.

L. M. G.

ANTENATAL AND POSTNATAL CARE.—By Francis J. Browne, M.D. (Aberd.), D.Sc., F.R.C.S. (Edin.), F.R.C.O.G. Sixth Edition. 1946. J. and A. Churchill Limited, London. Pp. viii plus 644, with complete index and 90 illustrations in the text. Price, 25s.

This is a book very well known to all medical students as one of the most important textbooks. In this latest edition the book has been revised throughout. Alteration has been chiefly made in the chapters on erythroblastosis and the Rh factor, on placenta prævia, toxæmias of late pregnancy and venereal diseases in pregnancy giving the current conception of all factors in their connection. Short sections have been added on acroparæsthesia, angular pregnancy and on the influence of Rubella and other infectious diseases in causing congenital abnormalities.

This edition no doubt will be very much valued by students and teachers alike, just as all other editions always have been valued in the past.

A. B.

GROWTH AND DEVELOPMENT OF THE YOUNG CHILD.—By W. Rand, A.B., R.N., M. E. Sweeney, A.M., M.S., and E. L. Vincent, Ph.D. Fourth Edition. 1946. W. B. Saunders Company, Limited, Philadelphia and London. Pp. vii plus 481. Illustrated. Price, 15s.

This book deals with the subject in greater detail than the name suggests. It gives full description of factors influencing, and up to date and best approaches to help the growth and development of the young child in the different fields (such as physical, intellectual, emotional and social, etc.) in the different phases of development. It also deals with some of the important social problems (as we find under the heading 'Importance of the family as a social institute', 'Change taking place in the family' and the various problems arising out of them), having serious effect on the growth and development of the young child of the modern society. The items dealt with under the heading 'Requisitions for satisfactory family life' will be very eagerly read by all men and women and no doubt will be very much appreciated. The book will prove to be of special value to all earnest workers in this field and students of this subject who have real interest in their work and study, to keep them abreast of the results of the latest investigations and observations in this field, and current conceptions of growth and developments of the young child.

A. B.

THE RESULTS OF RADIUM AND X-RAY THERAPY IN MALIGNANT DISEASE. SECOND STATISTICAL REPORT FROM THE HOLT RADIUM INSTITUTE, MANCHESTER, 1934-38.—Compiled by Ralston Paterson, Margaret Tod and Marlon Russell. E. and S. Livingstone Limited, Edinburgh. 1946. Pp. 147. Price, 7s. 6d. Postage, 5d. (home)

The names of the authors are a sufficient guarantee for the quality of this compilation.

The report is divided into three parts. The first part—a general survey of the treatment of malignant disease as a whole, intended to interest everyone including the layman, the administrator concerned with hospital organization, and the general practitioner. It consists of a survey by site of the results of radiotherapy in malignant disease, e.g. skin, mouth and lips, breast, etc. Short commentaries are given on each group, which are couched in simple language, and should be most illuminating to all concerned.

The second part is an analysis in which an attempt is made to evaluate different methods of treatment. The techniques used are described shortly and a reference is made to publications in which a fuller account may be found.

The third part refers to the first report, and is interesting mainly as it gives a table showing the ten-year evaluation of the cases treated in 1932 and 1933 with explanatory comments.

The report as a whole provides a complete record of the work of the Holt Radium Institute for the five years since the first report, including the ten-year figures for 1932 and 1933. In addition, the follow-up covers the five-year period to the end of 1943.

Simplicity and brevity are the key-notes of this publication. It contains illuminating and valuable information on various aspects of the treatment of this scourge of humanity, much of it understandable to the layman as well as to the scientist and practitioner of medicine. It certainly should find a place on the bookshelf of every medical practitioner and specialist interested in this form of disease.

Moreover the price 7s. 6d. is very moderate.

J. A. S.

ROENTGEN DIAGNOSIS OF DISEASES OF THE GASTRO-INTESTINAL TRACT.—By John T. Farrell, Jr., M.D. 1946. Charles C. Thomas, Springfield, Illinois. Pp. ix plus 271, with 191 illustrations. Price, £1 10s. Available from Baillière, Tindall and Cox, London

The author, who is Clinical Professor of Surgery at the Graduate School of Medicine, University of Pennsylvania, has put his lecture notes into book form. He has at the outset adopted the standard classified nomenclature of disease of the American Medical Association, a numerical one. The method doubtless has its uses, particularly when the statistical machine is called for. Throughout the book, three radiological features are stressed, viz, alterations of motility, position and contour. Though like most books of this type the matter is rather concentrated, it is readable; and the post-graduate student preparing for an examination will find perusal of value. It is certainly not a book of reference, and in our opinion not complete enough for a D.M.R. examination.

The skiagrams are well reproduced—one, figure 133, is upside down.

S. G. G.

BULLETIN OF THE HEALTH ORGANIZATION, LEAGUE OF NATIONS. Vol. XII, No. 1, 1945-46. Published by Publications Department of the League of Nations, Geneva, Switzerland

Among the many useful programmes adopted by the Health Organization of the League of Nations, one of the outstanding ones has been the systematic efforts made towards the standardization of potent drugs by biological methods. The influence this has exerted in bringing order out of chaos in biological therapeutics of modern times is not sufficiently realized in many quarters. During the First World War, many lives

were lost as a result of using antitoxins of low titre manufactured in foreign countries because there was no international agreement about the 'standard potency' of such substances. The situation is very different now, thanks to the Health Organization and almost all the potent biologicals, hormones, vitamins, etc., no matter from what source or country they originate, are, more often than not, found to conform to the internationally-agreed standards of reference set up by the Committee on Biological Standardization of the League of Nations. The Bulletin of the Health Organization, by publishing the necessary data in this connection from time to time, has served as the most authoritative journal of reference in these matters.

The present issue (No. 1, Vol. XII, 1945-46) would be most welcome to those working in this field as this is one of the first post-war publications bringing the account of biological standardization from 1935 onwards up to date. Dr. Gautier, the Secretary to the Permanent Commission on Biological Standardization, has contributed the first chapter on 'Health Organization and Biological Standardization—Second Memorandum' and this is an admirable review of the present status of our knowledge on the subject. Dr. Hartley, the erstwhile Director of the Department of Biological Standards of the National Institute for Medical Research at Hampstead, London, has written about International Standards for Antitoxins and Antisera and also about International Standards for Drugs, Hormones and Vitamins. The last chapter deals with the Interim Report of the Technical Commission of Pharmacopœia Experts on the Unification of Pharmacopœias, drawn up by Dr. Hampshire, Secretary of the British Pharmacopœia Commission and Chairman of the International Technical Commission. The material presented therefore is most authoritative and instructive. All routine and research laboratories dealing with drugs and pharmaceuticals in this country should try to possess a copy of this number of the Bulletin. The details given are very helpful and the monographs on some potent remedies adopted for the International Pharmacopœia are likely to be acceptable also to those countries which are not at present signatories to the League of Nations, and who do not possess a National Pharmacopœia of their own. In fact, if this scheme of the unification of pharmacopœias is pushed vigorously during the next few post-war years, there would be no need for 'National Pharmacopœias' and confusion from diversity of standards from one country's pharmacopœia to another would be a thing of the past.

B. M.

BOOKS RECEIVED

1. The Genus *Ixodes* in North America. By R. A. Cooley and Glen M. Kohls. National Institute of Health Bulletin No. 184. Published by Federal Security Agency, U.S. Public Health Service, Washington, D.C.
2. Venereal Disease Control. (Post-war): Proceedings, National Conference. St. Louis, Missouri, November 1944. Supplement No. 20 to the Journal of Venereal Disease Information. Published by Federal Security Agency, U.S. Public Health Service, Washington, D.C.
3. Nutrition. Bulletin No. 20, August 1946. Published by the Department of Food, Government of India, New Delhi.
4. Nutrition. Bulletin No. 21, September 1946. Published by the Department of Food, Government of India, New Delhi.
5. Catalogue (1946) of Lippincott Medical Publications for the Medical, Dental, Nursing, Pharmacy and Allied Professions. Export Edition. Published by J. B. Lippincott Company, Philadelphia and London.
6. Annual Report by the Curator of the Laboratory of the Royal College of Physicians of Edinburgh for the Year 1945.
7. Thirty-Fourth Conference of the All-India Medical Licentiate's Association. Presidential Address by Dr. Manoharlal Kapur, Poona, 19th October, 1946.

Abstracts from Reports

ANNUAL REPORT OF RESEARCH (1945) OF THE COLLEGE OF THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN

In a twenty-page pamphlet, a record of research work completed and published during the session 1944-45 in the various departments of the College of the Pharmaceutical Society has been presented with a foreword by the Dean, Professor H. Berry. The account forms stimulating reading particularly when it is considered that during the major part of the year the war clouds were still hanging over Britain and the environment was far from ideal as far as research work was concerned.

The activities of the institution are presented as contributions from five departments:—(a) Department of Pharmaceutics, (b) Department of Pharmaceutical Chemistry, (c) Department of Pharmacognosy, (d) Department of Pharmacology, and (e) Department of Nutrition. In the Department of Pharmaceutics under the direction of Professor Berry, research work was continued on methods of evaluating disinfectants, antiseptics and fungicides. The Department of Pharmaceutical Chemistry under Professor Linnell took up work in connection with the separation of the stereoisomers of reduced resorcinol and the use of the dihydroxy-benzenes as components in sulphonamide compounds. The study of cardamom seed was intensively pursued in the Pharmacognosy Laboratory under Dr. Wallis and tables for the identification of the seeds, based on their numerical and structural studies conducted, were prepared. A very useful and convenient method of digitalis assay on guinea-pigs was examined in the Department of Pharmacology along with investigations on the stability and toxicity of commercial adrenaline solutions. This latter study is laying the foundation for the elaboration of a method for the preservation of adrenaline solutions which are notorious for quick deterioration in potency. In the Department of Nutrition under Dr. Coward, worth-while contributions have been made on the human requirement of vitamin A and vitamin C. In addition, routine tests of the vitamin D content of margarines, cod-liver oil and cod-liver oil compounds were carried out for the Ministry of Food.

B. M.

Correspondence

PHARMACY BILL

SIR,—That the Bill as presented before the Central Legislature is very much defective has been admitted in all responsible quarters and all those interested have had their say and suggested improvements to the Bill. But Dr. R. Chatterji (*I.M.G.*, p. 334, Aug. '46) has hit off the mark in criticizing the Provincial State Medical Faculties. They are at best examining bodies. They have no powers to remove quackery. That is the duty of the Legislatures. In Bombay, for example; of all provinces of India, we have the Indigenous Medical Practitioners' Act, 1938, under which all those medical men—qualified or unqualified—practising on a certain date were registered or enlisted and allowed to continue their practice. But after the date no one can practise unless he is qualified. The British Medical Act of 1857 was also enacted on these lines. It is only by passing similar acts that quackery can be eradicated from the land. Similarly the profession of Pharmacy should be benefited, as under the Bill no unqualified man would be allowed either to be a pharmacist or a dispenser or compounder after the passing of the Bill and enforcement of the Act.

Yours faithfully,
U. B. NARAYANRAO.

BOMBAY, 4.

Any Questions

TREATMENT FOR ALOPECIA

SIR,—I shall be grateful if you will advise me through your answer column as to what may be done for the cure of alopecia in a girl aged 20.

9, DURAND ROAD,
LAHORE.

Yours, etc.,

(Sd.) SARDUL SINGH.

- I. Exclude psychoneurosis first—the condition called 'Trichotillomania'—a bad habit of tearing off the hair by hysterical young women, because of the supposed local irritation. Treatment is mainly psychological. Also a good general tonic and local application of a mild antiseptic lotion or ointment with 2 to 3 per cent phenol.
- II. Alopecia or baldness along with or after a debilitating disease, *e.g.* enteric, anaemia, and during lactation. The primary condition should be treated first, followed by a good general tonic to improve the health. Locally—ultra-violet irradiation to the patches and stimulating applications (*vide* alopecia areata). In obstinate cases—anterior pituitary extract injections or polyvalent gonads orally.
- III. Syphilitic alopecia—giving a sort of moth-eaten appearance to the scalp. Blood examination easily confirms the diagnosis. Vigorous anti-syphilitic treatment cures the condition. Local application may be given only to satisfy the patient.
- IV. Lupus erythematosus—Alopecia due to scar of the resultant ulceration. The diagnosis is easy from the presence of ulcers or scars on the scalp and also lupus ulcers elsewhere in the body. Treatment of lupus condition and application of soothing application.
- V. Seborrhoeic alopecia (pityriasis capitis). This is a very rare condition in women. The presence of dandruff on the scalp is easily detected. Treatment for seborrhoeic condition of the scalp for a prolonged period.
- VI. Alopecia areata—This is the commonest condition. In this a small patch of alopecia makes its appearance all of a sudden, the hair falling off and leaving a smooth glossy surface. This bald patch goes on increasing and other patches might appear in the scalp.

Treatment.—Search very carefully for any possible local sepsis in the teeth, throat, tonsils, nasal sinuses, bowels and pelvis. Treat the septic condition effectively. Ultra-violet light therapy is of great benefit. Stimulant applications mentioned below should be rubbed vigorously once or twice a day. Local injections intradermally of milk one or two drops for each area of one square centimetre twice weekly has been found useful. In obstinate cases anterior pituitary extract or polyvalent gonads may be tried.

Some stimulant applications :

R		R	
Tr. capsici ..	dr. i	Liq. ammon. fort.	℥xv
Tr. cantharidine ..	dr. i	Tr. cantharidine ..	dr. ½
Glycerine ..	dr. i	Tr. capsici ..	dr. ½
Aqua rose ..	to 1 oz.	Aqua rose ..	to 1 oz
Ft. lotion—to apply.		Ft. lotion—to apply.	

2 to 5 per cent ung. chrysarobin or ung. derobin to rub on the patches occasionally. It is important that the patient be warned to be very careful that the drug or the finger touching the ointment does not reach the eyes.—I.M.G.]

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL SIR G. COVELL, C.I.E., K.H.P., resumed charge of the post of Director, Malaria Institute of India, on the afternoon of the 17th July, 1946, on completion of his deputation to the United Kingdom and the United States of America.

The Governor is pleased to reappoint Major-General W. E. R. Dimond, C.I.E., C.B.E., K.H.P., on return from leave, as Surgeon-General with the Government of Bengal, *vice* Lieutenant-Colonel C. L. Pasricha.

Colonel L. K. Ledger, O.B.E., on return from 4 months' leave *ex-India*, assumed charge of the Inspector-General of Civil Hospitals, Central Provinces and Berar, with effect from 21st October, 1946.

Lieutenant-Colonel (Temporary Colonel) A. K. Sahibzada, O.B.E., was appointed to officiate as Deputy Director-General, Indian Medical Service, from the 27th December, 1944, to the 30th April, 1945, and to hold the post substantively, with effect from the 1st May, 1945, *vice* Colonel S. L. Bhatia, M.C.

Lieutenant-Colonel K. S. Fitch, O.B.E., Assistant Director-General, Indian Medical Service (Resettlement), is appointed Additional Deputy Director-General, Indian Medical Service (Resettlement), with effect from the 26th April, 1946.

Lieutenant-Colonel M. K. Afridi, O.B.E., Deputy Director, Malaria Institute of India, was placed on deputation to the United States of America from the 3rd June, 1946.

Lieutenant-Colonel W. T. Taylor, Officer on Special Duty in the office of the Director-General, Indian Medical Service, is appointed to officiate as Additional Deputy Director-General, Indian Medical Service (Stores), with effect from the afternoon of the 4th June, 1946, *vice* Lieutenant-Colonel M. K. Kelavkar, O.B.E., granted leave.

Lieutenant-Colonel W. H. Crichton, C.I.E., Director of Public Health, Central Provinces and Berar, is appointed to officiate as Inspector-General of Civil Hospitals, Central Provinces and Berar, in addition to his own duties, with effect from the 13th June, 1946.

Lieutenant-Colonel W. Scott on return from leave was placed as Officer on Special Duty in the office of the Inspector-General of Civil Hospitals, Central Provinces and Berar, with effect from the 17th June, 1946, to the 23rd June, 1946 (both days inclusive), and then assumed charge as Civil Surgeon, Nagpur, from the 24th June, 1946.

Lieutenant-Colonel W. J. Webster, M.C., Assistant Director, Central Research Institute, Kasauli, is appointed to officiate as Director of that Institute, with effect from the afternoon of 6th July, 1946, *vice* Lieutenant-Colonel H. W. Mulligan.

Lieutenant-Colonel R. H. Malone, I.M.S. (Retd.), has been appointed temporarily as Assistant Director, Central Research Institute, Kasauli, from the afternoon of the 6th July, 1946.

Lieutenant-Colonel T. S. Shastri, I.M.S. (Retd.), was relieved of his duties as Director, Government of India Medical Mission (Malaya), with effect from the afternoon of the 20th July, 1946.

Lieutenant-Colonel Jaswant Singh, Deputy Director, Malaria Institute of India, was appointed to officiate as Director, Malaria Institute of India, in addition to his own duties during the absence on deputation of Major-General Covell.

Lieutenant-Colonel S. L. Patney made over charge of the Presidency Jail to Major E. A. R. Ardeshir, in the forenoon of the 8th June, 1946.

Lieutenant-Colonel C. L. Pasricha, Surgeon-General, with the Government of Bengal, on relief, reverts to his substantive post of Professor of Pathology and Bacteriology, School of Tropical Medicine, Calcutta, *vice* Dr. Ganapati Panja.

Lieutenant-Colonel R. Linton, doing general duty at the office of the Surgeon-General with the Government

of Bengal, is appointed to be Principal, Medical College, and Superintendent of the Medical College Hospitals, Calcutta, *vice* Lieutenant-Colonel E. G. Montgomery. Lieutenant-Colonel W. H. Crichton, C.I.E., Director of Public Health, C. P. and Berar, ceased to hold additional charge of the Inspector-General of Civil Hospitals, C. P. and Berar, with effect from 21st October, 1946.

Lieutenant-Colonel F. R. W. K. Allen, Officer on Special Duty in the office of the Inspector-General of Civil Hospitals, C. P. and Berar, is posted as Civil Surgeon, Amraoti, with effect from the 25th October, 1946.

The Secretary of State for India has appointed to the Indian Medical Service (Civil) the following officers of the Indian Medical Service, with effect from the dates stated against their names :—

Central Government

Major C. Mani. Dated 3rd February, 1945.

Major T. C. Puri. Dated 20th April, 1945.

Bengal

Captain E. J. Somerset. Dated 18th May, 1944.

Major W. J. Virgin. Dated 15th October, 1944.

Bihar

Major A. N. Duggal. Dated 19th October, 1944.

Assam

Major T. D. Ahmad. Dated 30th October, 1944.

Punjab

Captain M. D. Black. Dated 2nd February, 1945.

The undermentioned Indian Medical Service (Civil) Officer is reverted to the Burma Establishment, with effect from the date shown against his name :—

Major S. W. Allinson. Dated 4th April, 1946.

Major B. Temple-Raston, Deputy Inspector-General of Civil Hospitals, Punjab, is appointed Civil Surgeon, Simla East, with effect from the afternoon of the 30th April, 1946.

Major S. P. Ramakrishnan is appointed to officiate as Assistant Director, Malaria Institute of India, Delhi, with effect from the afternoon of the 18th May, 1946, until further orders.

Major H. A. Ledgard, Civil Surgeon, Quetta-Sibi, is appointed as Chief Medical Officer and Inspector-General of Prisons in Baluchistan, with effect from the afternoon of the 21st May, 1946, in addition to his own duties.

Major F. E. Buckler was appointed Additional Assistant to the Surgeon to His Excellency the Viceroy from the 2nd April, 1946, to the 28th May, 1946, and Assistant to the Surgeon to His Excellency the Viceroy from the 29th May, 1946, *vice* Major D. S. Jackson, granted leave.

Major D. P. Dewe is appointed as an Agency Surgeon substantively on probation with effect from the forenoon of the 9th June, 1946.

The following appointment is made on His Excellency the Viceroy's personal staff :—

Major F. E. Buckler, Assistant to the Surgeon to His Excellency the Viceroy, is appointed to officiate as Surgeon to His Excellency the Viceroy in addition to his own duties, with effect from the 1st August, 1946, *vice* Lieutenant-Colonel H. Williamson, O.B.E., I.M.S. (Retd.), granted leave *ex-India*.

Major W. J. Virgin, Civil Surgeon, Dacca, is appointed to be the Principal of the Medical College, and Superintendent of the Hospital, Dacca, with effect from the date on which he takes over charge.

Major G. B. W. Fisher, on return from leave, is appointed to be Professor of Clinical Midwifery and Gynaecology, Medical College, Calcutta, *vice* Dr. Sudhir Chandra Basu.

Major J. Goodall, doing general duty at the Medical College Hospitals, Calcutta, is appointed to be Professor of Clinical Medicine, Medical College, Calcutta, *vice* Dr. A. K. M. A. Wahed.

Major N. Z. Y. Hussain is appointed temporarily to the post of Assistant Officer-in-charge, Anti-Malaria Operations, Delhi, with effect from the 22nd August, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

To be Major

Husain Akhtar. Dated 22nd January, 1946.

Captain R. N. Sen was appointed to the temporary post of Malaria Officer, Raniganj, with effect from the 12th March, 1946.

Captain P. S. Bhargava has been appointed as Assistant to Medical Adviser (Pensions), War Department (Pension Branch), 19th March, 1946.

Captain G. H. F. Humphreys is appointed Civil Surgeon, Gangtok, with effect from the afternoon of the 9th April, 1946.

The undermentioned officers of the Indian Medical Service (E.C.) revert from the Indian Army Medical Corps and are seconded for service in the Royal Indian Air Force :—

Captain G. P. Ghosh. Dated 4th May, 1946.

Captain M. S. Khara. Dated 7th May, 1946.

Captain J. K. Sehgal. Dated 14th May, 1946.

Captain R. C. Sharma. Dated 15th May, 1946.

The services of Captain M. C. Sharma, Liaison Officer (Drugs) in the office of the Liaison Officer (Consumer Goods), Bombay, have been replaced at the disposal of the Director-General, Indian Medical Services, with effect from the afternoon of the 1st July, 1946.

Captain A. P. Ray is appointed temporarily as Assistant Director, Malaria Institute of India, with effect from the 1st August, 1946, until further orders.

Captain N. Jungalwalla is appointed temporarily as Additional Deputy Public Health Commissioner with the Government of India, with effect from the 8th August, 1946.

Captain R. Passmore, an Officer of the Medical Research Department, is appointed temporarily as Assistant Director, Central Research Institute, Kasauli, with effect from the 26th August, 1946.

Captain A. N. Roy is appointed as Deputy Assistant Director-General, Indian Medical Service (Resettlement), with effect from the 27th August, 1946.

Captain G. H. K. Niazi is appointed as Deputy Assistant Director-General (Medical Stores), Medical Store Depot, Raipur, with effect from the forenoon of 14th September, 1946.

The undermentioned officer of the Indian Medical Service (E.C.) reverts from the R.I.N.V.R. and is seconded to the Indian Army Medical Corps :—

Captain M. Bhattacharjee. Dated 16th February, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

To be Captain

Mohammed Hamid Mirza. Dated 15th May, 1944.

To be Lieutenants

3rd April, 1943

K. Venkataraman.

D. Sankaran.

T. R. Mainyan.

C. T. G. Tilak.

L. W. Mackey.

T. G. Jones.

R. D. Thorpe.

R. A. Garson.

The undermentioned officer of the Indian Medical Service (E.C.) reverts from the Indian Army Medical Corps and is seconded for service in the Royal Indian Air Force :—

Captain N. G. Govindaraj. Dated 17th May, 1946.

The undermentioned officer of the Indian Medical Service (E.C.) reverts from the Indian Army Medical Corps and is seconded for service in the Royal Indian Air Force :—

Captain S. K. Muhury. Dated 21st August, 1946.

LEAVE

Lieutenant-Colonel H. E. Murray, C.I.E., Professor of Midwifery, Medical College, Calcutta, is granted leave for 28 months preparatory to retirement by the Secretary of State for India.

Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C., an Agency Surgeon, is granted leave on average pay for 8 months combined with leave on half average pay for 20 months, with effect from the afternoon of the 21st May, 1946, pending retirement.

Lieutenant-Colonel M. K. Kelavkar, O.B.E., Additional Deputy Director-General, Indian Medical Service (Stores), is granted leave for 4 months (War concession leave for 24 days and the balance on average pay) with effect from the afternoon of the 4th June, 1946.

Major C. L. Greening, Assistant Director, Central Research Institute, Kasauli, is granted leave on average pay *ex-India* for 4 months under the Key Leave Scheme with effect from the afternoon of the 30th May, 1946.

Major R. D. MacRae, an Agency Surgeon, is granted leave for 6 months with effect from the forenoon of the 9th June, 1946.

Major T. Somerville, an officer of the Medical Research Department on foreign service under the Indian Research Fund Association, is granted leave on average pay *ex-India* for 6 months under the Key Leave Scheme with effect from the afternoon of the 11th June, 1946. His services are replaced at the disposal of the Director-General, Indian Medical Service, for the period of his leave.

Major G. P. Charlewood, Civil Surgeon, Ajmer, is granted leave on average pay *ex-India* for 6 months under the Key Leave Scheme with effect from the afternoon of the 13th June, 1946.

PROMOTIONS

Lieutenant-Colonel to be Colonel

J. Rodger, O.B.E., M.C. Dated 21st August, 1946.

The undermentioned Indian Medical Service Officer is advanced to the list of Special Selected Lieutenant-Colonel :—

Lieutenant-Colonel M. A. Singh. Dated 19th May, 1946.

Majors to be Lieutenant-Colonels

B. M. Rao. Dated 6th May, 1946.

B. N. Hajra. Dated 10th May, 1946.

R. M. Lloyd Still. Dated 17th May, 1946.

A. Singh. Dated 20th May, 1946.

K. F. Alford. Dated 6th July, 1946.

S. C. Bakhle. Dated 28th August, 1946.

7th September, 1946

P. J. Kelly. E. M. Swell.

Captains to be Majors

W. C. Taylor. Dated 1st November, 1944.

1st May, 1946

L. S. F. Woodhead. W. C. Templeton.

J. R. Kerr. G. W. Palmer.

J. D. Munroe. B. J. Doran.

T. M. Williams.

R. B. Davis. Dated 12th June, 1946.

W. M. Wilson. Dated 1st July, 1946.

31st August, 1946

W. A. Hopkins. L. U. Kamm.

J. W. R. Sarkies. T. Donness.

F. M. Byrn.

W. Laurie. Dated 10th September, 1946.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Captain to be Major

B. Bhattacharjya. Dated 12th January, 1946.

LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commissions)

Captains to be Majors

Krishnadhan Banerjee. Dated 15th November, 1945.

P. Chandra. Dated 7th January, 1946.

H. Dhawan. Dated 15th January, 1946.

N. S. Pillay. Dated 2nd February, 1946.

Kunnathur Parthasarathy. Dated 28th February, 1946.

M. Krishnamurthi. Dated 1st April, 1946.

M. A. Haq. Dated 8th April, 1946.

5th May, 1946

K. Abraham.

G. A. Roche.

K. S. Bagchi.

B. S. Patankar.

R. S. Gupta.

S. C. Ghosh. Dated 13th May, 1946.

D. R. Bharucha. Dated 18th May, 1946.

R. A. Davar. Dated 19th May, 1946.

12th July, 1946

B. Bhattacharjya.

M. B. Menon.

G. H. K. Niazi.

E. L. Jones. Dated 21st August, 1946.

LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Captains to be Majors

D. C. Logan. Dated 31st December, 1945.

1st February, 1946

G. S. Sandhu.

M. D. Joshy.

E. B. Mody.

P. P. Hazari.

M. M. Hossain. Dated 3rd February, 1946.

5th February, 1946

T. D. Narang.

A. A. Rawat.

M. N. Ghosh. Dated 6th February, 1946.

M. B. Hasan. Dated 8th February, 1946.

15th February, 1946

M. S. Hashemi.

N. Khansur.

P. N. Roy.

B. C. Singh. Dated 17th February, 1946.

J. M. Murray. Dated 21st February, 1946.

1st March, 1946

C. M. Menon.

M. Z. Y. Hussain.

K. N. Sen. Dated 4th March, 1946.

5th March, 1946

L. A. Venkataraman.

V. B. Kale.

V. S. Mahadevan.

S. M. Apte. Dated 6th March, 1946.

S. R. Chowdhury. Dated 14th March, 1946.

N. G. Kar. Dated 16th March, 1946.

L. R. S. Deo. Dated 20th March, 1946.

V. Swaminathan. Dated 22nd March, 1946.

23rd March, 1946

C. L. Chadda.

G. C. Chawla.

S. K. Bose. Dated 29th March, 1946.

G. McCracken. Dated 4th April, 1946.

T. S. Chohan. Dated 6th April, 1946.

A. K. Gupta. Dated 7th April, 1946.

9th April, 1946

E. D. MacWorth.

G. R. Butterfield.

12th April, 1946

K. P. Mukerji.

A. P. Bannerjee.

13th April, 1946

N. R. Gupta.

A. T. George.

A. N. Subbarama.

M. B. Thakure. Dated 18th April, 1946.

G. L. Dutt. Dated 21st April, 1946.

Lieutenants to be Captains

11th February, 1946

M. Nazir.

A. R. Ray.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Lieutenants to be Captains

Harbans Singh Gill. Dated 23rd August, 1945.

T. P. Sharma. Dated 10th December, 1945.

K. Satyashankar. Dated 1st February, 1946.

6th February, 1946

S. T. Ohol.

T. Acharyya.

12th February, 1946

B. K. Basu.

S. A. Rahman.

B. R. Mukherjee.

M. A. S. Khan. Dated 13th February, 1946.

P. K. Mishra. Dated 14th February, 1946.

M. A. Rozalla. Dated 19th February, 1946.

21st February, 1946

B. S. Manocha. Z. Mian.
S. K. Saigol.

J. S. Patheja. Dated 22nd February, 1946.
C. D. Kalra. Dated 23rd February, 1946.
P. K. Ray Chaudhuri. Dated 7th March, 1946.
K. M. Banik. Dated 12th March, 1946.
K. Seetaram. Dated 13th March, 1946.
D. K. Sen. Dated 17th March, 1946.
D. K. Basu. Dated 26th March, 1946.
B. S. Narayanaswamy. Dated 28th March, 1946.

29th March, 1946

N. R. Banerjee. D. N. Roy.
P. P. S. Menon. Dated 26th April, 1946.
N. C. Das. Dated 27th April, 1946.

RETIREMENTS

Lieutenant-Colonel C. S. V. Ramanan. Dated 25th January, 1946.

Lieutenant-Colonel (T/Col.) D. N. Bhaduri, 6th August, 1946, and is granted the honorary rank of Colonel.

The undermentioned officer retired with gratuity from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Short Service Commission)

Captain H. Akhtar. Dated 22nd January, 1946.

RESIGNATIONS

The undermentioned officers are permitted to resign their commissions :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain K. C. Chaudhuri. Dated 13th March, 1946.
Captain V. S. Ramaswami. Dated 12th June, 1946.

The undermentioned officer is permitted to resign his commission :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain M. M. R. V. A. Nambiyar. Dated 5th July, 1946.

RELINQUISHMENT

Lieutenant-Colonel G. H. Fraser, Medical Adviser (Pensions), War Department (Pensions Branch), relinquished the appointment. Dated 15th April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Lieutenant-Colonel :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major D. P. Puri. Dated 18th March, 1946.

Lieutenant-Colonel N. F. Lilauwala. Dated 16th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Lieutenant-Colonel :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

(Ty.) Lieutenant-Colonel G. V. Chaphekar. Dated 11th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Lieutenant-Colonel. His services are replaced at the disposal of the Government of Madras with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Lieutenant-Colonel C. K. P. Menon. Dated 1st August, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Lieutenant-Colonel :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Lieutenant-Colonel D. R. Bharucha. Dated 7th August, 1946.

INDIAN MEDICAL SERVICE
(Emergency Commissions)

Major J. T. Prendiville relinquishes his commission on account of ill health, dated 14th August, 1945, and is granted the honorary rank of Major.

Major A. R. Woodforde, Medical Adviser (Pensions), War Department (Pensions Branch), relinquished the appointment. Dated 22nd March, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Major H. C. Dhawan. Dated 8th March, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major and his services are replaced at the disposal of the Government of the United Provinces from the date specified :—

INDIAN MEDICAL SERVICE—INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major A. Ahmed. Dated 15th March, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Ty. Major J. S. Rao. Dated 26th March, 1946.

Major P. M. Bhandarkar. Dated 13th April, 1946.

Major S. B. Lal. Dated 15th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major. His services are replaced at the disposal of the Government of Madras with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Major V. Swaminathan. Dated 4th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major. His services have been replaced at the Government of U. P. with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Major Mohammad Anwarul Haq. Dated 10th April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Major R. C. Bose. Dated 17th April, 1946.

Ty. Major B. S. Dhillon. Dated 18th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major J. R. Sen. Dated 18th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major. His services are replaced at the disposal of the Government of Bengal from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major Sudhansu Mohan Ghosh. Dated 23rd April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service, and is granted the honorary rank of Major, subject to His Majesty's approval :—

LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Ty. Major C. H. Phillips. Dated 26th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Ty. Major D. A. Pundlik. Dated 26th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major. His services are replaced at the disposal of the Bengal Government with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major S. K. Ganguli. Dated 29th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major C. D. Torpy. Dated 30th April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major. Their services are replaced at the disposal of the Government of Bihar with effect from the dates specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major H. N. Sahay. Dated 3rd May, 1946.

Major Amalendu Chatteraj. Dated 15th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major. Their services are replaced at the disposal of the Government of the United Provinces from the dates specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major J. N. Jaswal. Dated 29th April, 1946.

Ty. Major B. W. Lyall. Dated 18th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major R. S. Rao. Dated 1st May, 1946.

L. C. R. Emmett. Dated 5th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major S. C. Ray. Dated 29th May, 1946.

Ty. Major P. Banerje. Dated 19th June, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major Shambhu Nath Aggarwal. Dated 12th September, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major C. F. Vieyra, M.B.E. Dated 24th October, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major V. R. Kamath. Dated 1st May, 1946.

Captain R. R. Reddy. Dated 5th May, 1946.

The undermentioned officer is permitted to relinquish his commission on reversion to the Indian State Forces :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain M. Z. Hasan. Dated 4th February, 1946.

The undermentioned officer is permitted to relinquish his emergency commission and is reverted to his former and entitled status in the I.A.M.C. (S.M.S.) :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain K. E. R. Robertson. Dated 3rd March, 1946.

The undermentioned officer is permitted to relinquish his commission on reversion to the Indian State Forces :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain M. A. Rauf. Dated 26th March, 1946.

The undermentioned officer is permitted to relinquish his emergency commission on release from army service :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain M. D. Innis. Dated 1st April, 1946.

The undermentioned officer is permitted to relinquish his commission on reversion to the Indian State Forces :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain K. P. N. Panicker. Dated 6th May, 1946.

The undermentioned officer is permitted to relinquish his commission :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain Abdul Jabbar. Dated 31st August, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are replaced at the disposal of the Government of C. P. and Berar from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain B. R. Kashyap. Dated 3rd April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain M. Habibullah. Dated 6th April, 1946.

Captain Samuel Sindha Ram Singh. Dated 9th May, 1946.

Captain J. G. Rodrigues. Dated 14th June, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain. Their services are replaced at the disposal of the Government of United Provinces with effect from the dates specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain H. S. Saksena. Dated 20th April, 1946.

Captain P. C. Roy Asawarival. Dated 24th April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain C. C. Menon. Dated 9th April, 1946.

Captain N. B. Das Gupta. Dated 20th April, 1946.

Captain V. N. Khanna. Dated 27th April, 1946.

Captain V. P. Naidu. Dated 19th May, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are replaced at the disposal of the Government of U. P. from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain J. B. Singh. Dated 23rd April, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain J. Singh. Dated 26th April, 1946.

Captain R. I. Ananthanarayanan. Dated 26th May, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are replaced at the disposal of the United Provinces Government with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain S. S. Goyal. Dated 27th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are placed at the disposal of Bihar Government with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain B. Mukopadhaya. Dated 4th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain S. Maragathavel. Dated 19th April, 1946.

Captain M. V. Kurian. Dated 26th April, 1946.

Captain G. P. Halder. Dated 5th May, 1946.

Captain N. V. Subrahmanyam. Dated 17th May, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain S. Padmanabhan Iyer. Dated 25th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain G. D. Agarwal. Dated 3rd May, 1946.

Captain C. K. Ramchandar. Dated 18th June, 1946.

Captain Kona Chandra Rao. Dated 16th July, 1946.

Captain M. S. Venkat Raman. Dated 27th July, 1946.

Captain S. Hasan. Dated 31st July, 1946.

(WOMEN'S BRANCH)

Captain (Miss) B. Natarajan. Dated 30th July, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain P. K. Dhar. Dated 31st May, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are replaced at the disposal of Government of Orissa from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain B. K. Acharyya. Dated 1st June, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain L. J. Michael. Dated 4th June, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain H. Ghosal. Dated 7th April, 1946.

Captain G. S. Ramalu. Dated 2nd May, 1946.

Captain P. K. Sen. Dated 13th June, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain. His services are placed at the disposal of the Government of Bombay with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain D. N. Muzumdar. Dated 18th June, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain A. Satyanarayana. Dated 8th July, 1946.

The undermentioned officer is permitted to relinquish his commission on grounds of ill health and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain D. M. Kar. Dated 23rd July, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain S. M. Ghosh. Dated 31st July, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain N. Vythianathan. Dated 26th August, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain R. N. Sinha. Dated 24th May, 1946.

Captain C. R. Chandrasekhar. Dated 12th July, 1946.

Captain M. K. R. Panicker. Dated 30th July, 1946.

Captain S. C. Ghosh. Dated 6th August, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE ROYAL INDIAN NAVY
(Emergency Commission)

Captain M. A. Choudhrie. Dated 25th June, 1946.

SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain M. B. R. Khan. Dated 9th July, 1946.

Captain R. M. Gopalaratnam. Dated 9th July, 1946.

Captain K. N. Baria. Dated 19th July, 1946.

(WOMEN'S BRANCH)

Captain (Mrs.) M. F. Hutton. Dated 8th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Captain :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain S. V. Joseph. Dated 25th May, 1946.

Captain (Mrs.) Hamida K. Ahmad (née Malik). Dated 30th May, 1946.

Captain S. R. Chatterji. Dated 11th June, 1946.

Surgeon-Lieutenant P. K. N. Kishore. Dated 21st July, 1946.

Captain Inder Sen Jetley. Dated 25th July, 1946.

Captain N. G. Roy. Dated 29th July, 1946.

Captain K. Venkataraman. Dated 26th August, 1946.

(WOMEN'S BRANCH)

Captain (Mrs.) Kamla Rahim Khan (née K. Isaac). Dated 6th August, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Surgeon-Lieutenant :—

INDIAN MEDICAL SERVICE
SECONDED TO THE ROYAL INDIAN NAVY
(Emergency Commission)

Surgeon-Lieutenant Sarosh Bhacca. Dated 3rd May, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Surgeon-Lieutenant :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE ROYAL INDIAN NAVY
(Emergency Commission)

Captain H. B. Sinha. Dated 27th June, 1946.

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Original Articles

SULPHAPYRIDINE ANURIA INCLUDING HISTOPATHOLOGICAL EXAMINATION OF KIDNEY IN ONE CASE

By B. L. RAINA

MAJOR, I.M.S./I.A.M.C.

DURING the years 1944 and 1945 seven cases of sulphapyridine anuria were referred to this hospital from out stations. Two cases were treated medically and both recovered. Five were treated surgically by nephrostomy, out of which three died and two made a rapid recovery.

Clinical Features

All (except one) were healthy young Gurkhas. All necessary precautions were taken in every case. Their urines were alkaline, intake of fluids was satisfactory, quantity of sulphapyridine given was not excessive (one gramme four-hourly on the first day and one gramme six-hourly on the following day). Oliguria and later anuria were noticed on about the fifth day after starting the drug. Blood pressure and blood urea gradually started to rise (in the case under report blood pressure 145/100, blood urea 48 mg. per cent) and the patients became comatose.

Pathological Appearances

In the five cases in which nephrostomy was performed kidneys were found slightly enlarged, the capsule was adherent. On incision sero-sanguineous fluid 4 to 5 c.cm. exuded.

In the case in which autopsy was done oedematous patches were seen in the pelvis of the kidney (figure 1, plate XXXI). The ureters were acutely congested; bladder was empty and hæmorrhages were seen in the pelvis of the kidney, ureters and trigone of the bladder.

The sections of the kidney were examined by Dr. R. G. Dhaygude and Major K. Banerji. Their report is as follows:—

'Cortical portion: glomeruli more cellular than normal, capillaries markedly engorged; serofibrinous transudate present in the capsular space, some of which contain a few RBCs; capsular epithelium shows proliferation here and there. In some instances capsular space is almost obliterated. The epithelium of the uriniferous tubules show cloudy changes and their lumens contain serofibrinous transudate. Epithelium of proximal convoluted tubules and of the descending limbs of Henle is desquamated and detached *en bloc* as epithelial casts here and there, interstitial vessels are engorged and free RBCs are to be seen in some of the uriniferous tubules. There is no evidence of focal round cell infiltration.

Medullary portion: epithelium of loops of Henle and straight tubules are normal; their lumina contain serofibrinous transudate; the vasa recta are engorged. Some foci of necrosis are also to be seen in the medullary portion' (Banerji). 'The capsular spaces contain fluffy eosinophile deposit. Some of the tubules show in their inferior bluish-stained rounded slightly irregular bodies which, on closer examination, appear to be made up of a crystalline material (see figures 2 and 3, plate XXXI)

which has been bound together by an albuminous coating. These bodies are present mostly in the collecting tubules' (Dhaygude).

Intradermal Tests for Allergy

Sulphapyridine was given to a healthy person one gramme four-hourly; on the second day his serum was collected and 2 c.cm. was injected intradermally in the forearm of the recovered anuria cases and of controls. No reaction except slight erythema disappearing after 2 hours was noticed in the controls. In the two Gurkhas (recovered anuria cases) a weal 2 inches in diameter developed after 20 minutes and persisted for 24 hours.

Discussion

Three questions arise: (a) Was anuria in the above cases due to mechanical obstruction of urinary passage by sulphapyridine crystals? (b) Was it due to direct action of the drug? (c) Was it due to allergy? There is no doubt that glomerular filtrate is absorbed in the tubules and crystals can be precipitated if conditions are suitable. In the above cases urine was alkaline, intake of fluids and dosage of sulphapyridine were satisfactory. No gross mechanical obstructions were seen. Some tubules showed in the interior slightly irregular bodies which on closer examination appeared to be made up of crystalline material. The pathological picture was of glomerulo-tubular nephritis. It would appear that the damage was partly due to the direct action of the crystals on the collecting tubules. The capillary dilatation, transudation without any inflammatory mobilization, the positive skin reaction after injecting the sulphapyridine serum in the recovered cases, incidence of anuria in Gurkhas only (in the area a large number of troops, British, Italian and Indian, were given sulphapyridine without any anuria) suggest an allergic factor, but the number of cases on which intradermal tests were tried is too small to draw any general conclusions. It may however be recalled that allergic skin reactions amongst cases taking the sulpha group of drugs are well known. It is interesting to note that Barnes and Kawaichi observed that out of 40 Japanese in Los Angeles, 15 per cent developed anuria from sulphapyridine. Major Khan, surgical specialist, Peshawar District, informed me that the only case of sulphapyridine anuria he saw was in a Garhwale. It is possible that certain races are hypersensitive to the sulpha group of drugs.

Cases have been reported of sulphapyridine allergy and possibilities of desensitization have lately been discussed by various workers.

Summary

1. Cases of sulphapyridine anuria have been described.
2. The pathological picture is one of glomerulo-nephritis with evidence of damage to

the collecting tubules probably due to the presence of crystals of sulphate group of drugs.

3. Certain individuals and races (Gurkhas) may be hypersensitive to the drug.

I am grateful to Dr. R. G. Dhaygude, M.D., Professor of Pathology, G. S. Medical College, Bombay, and Major K. Banerji, I.M.S./I.A.M.C., for their valuable help and advice, and to the D.M.S. in India for his permission to publish the case.

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ENICOSTEMA LITTORALE BLUME IN MALARIA

By B. B. RAI, M.B., B.S.

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THE amount of cinchona alkaloids and other antimalarials falls far short of India's requirements. The recent introduction of synthetic antimalarials has been a welcome relief. Besides in day-to-day clinical practice it has been observed that patients would like to be treated with indigenous herbs or their decoctions in preference to quinine and its derivatives or the synthetic antimalarials which are not infrequently fraught with danger unless used under supervision of a qualified medical person whose dearth (1 doctor to 6,000 people) is well known.

Attempts were, therefore, made to find out some suitable indigenous antimalarials from the commonly growing plants which could be within the reach of a large number of persons.

Several plants were tried but the description and experiments with *E. littorale* Blume which was found to exercise a favourable effect are given below :

Description of the Plant

The plant was identified by the late Dr. Kashyap, Professor of Botany, Government College, Lahore, as *E. littorale* Blume (chhota chiraita) of the family Gentianaceæ. A diagrammatic sketch of the plant is given (see illustration).

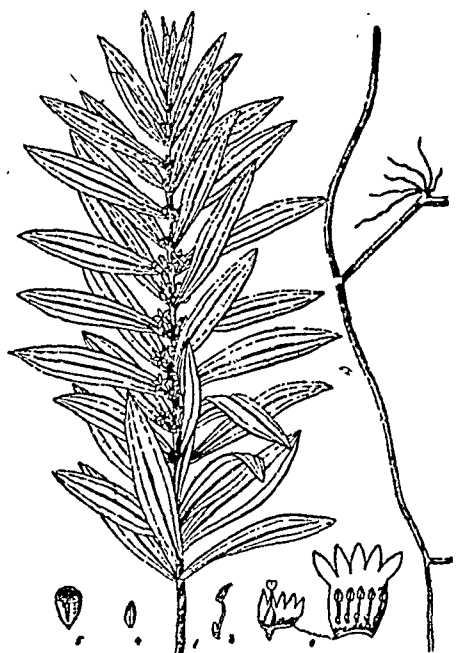
Habitat.—Common in wet places, more frequent near the sea.

Found throughout India up to an altitude of 1,500 ft. from the Punjab and Gangetic plains to Ceylon, though not known in Bengal.

Root.—Creeping and filiform.

Stem.—4 to 20 inches, terete or quadrangular, inter nodes short; several in number from a woody base, erect or procumbent, glabrous.

Leaves.—2 by $\frac{1}{2}$ inch or smaller, opposite, oblong oval to oblong linear, sessile, tapering to base, obtuse rather thick, three nerved, the



Enicostema littorale.

lateral nerves marginal and faint, pale glaucous green.

Flowers.— $\frac{1}{5}$ inch long, white or bluish in sessile, axillary clusters, calyx glabrous, segments lanceolate, subacute. Corolla much longer than the calyx, funnel-shaped, tubular, tube $\frac{1}{8}$ inch, lobes 5, much shorter than the tube, $\frac{1}{10}$ inch spreading, oblong with round ends. Stamens 5, on the upper part of corolla tube, filaments shortly linear with minute scales at their base; anthers oblong, acute, included. Ovary 1-celled, placenta not far intruded; style short, linear, stigma capital, capsule ellipsoid, carpels separating.

Seeds are small, many in number, reticulated and subglobose in shape.

The plant was collected in August and September in the flowering stage, dried in shade and made into powder.

Observations on human beings.—The selected subjects were uncomplicated cases of malaria with apparently good physique. They were reported to be having intermittent fever. Frank cases of malaria identified by blood smear examination were divided into B.T. and M.T. groups in September to October 1931 and supervised closely with the assistance of the civil surgeon and superintendent in charge of Lyallpur jail who were kind enough to provide prisoner patients for these trials. Similar observations were repeated in 1942 in Bareilly in my clinic. The usual procedure adopted in the treatment was the administration of 1 dram of powdered chhota chiraita three times a day after an initial saline purge on the previous evening. The administration was continued for 3

days after the disappearance of pyrexial conditions. Blood smears were examined daily during this period till the peripheral blood became parasite free. After discontinuing the treatment, the patients were watched for 6 weeks. Blood smears were examined every week to find out the percentage of relapse. Both at Lyallpur and Bareilly 32 cases were kept under observation. To save space protocols of 6 cases are given below :

PROTOCOL 1

Name	Age	Type of infection
Arshad	25	B.T. rings

(Temperature on arrival 104°F., given calomel at night followed by mag. sulph. at 5 a.m. next morning.)

2nd day.

3 doses of *E. l. Blume* given with lime water.

Temperature
8 a.m. 98.0°F.
2 p.m. 99.0°F.
5 p.m. 98.6°F.

3rd day.

3 doses of *E. l. Blume* given with lemon water.

Temperature
8 a.m. 98.4°F.
2 p.m. 98.2°F.
5 p.m. 99.0°F.

4th day.

3 doses of *E. l. Blume* given with lemon water.

Temperature
8 a.m. 98.2°F.
2 p.m. 98.4°F.
5 p.m. 98.0°F.

5th day.

3 doses of *E. l. Blume* given with lemon water.

Temperature
8 a.m. 98.2°F.
2 p.m. 98.0°F.
5 p.m. 97.2°F.

(Slide — ve.)

Discharged. No relapse noted within 6 weeks.

PROTOCOL 2

Name	Age	Type of infection
Ramesh	28	B.T. rings

(Admitted when temperature was 104.6°F., given calomel at night, followed by mag. sulph. in the morning.)

2nd day.

Given 3 doses of *E. l. Blume* with lemon water.

Temperature
8 a.m. 97.4°F.
2 p.m. 98.0°F.
5 p.m. 98.4°F.

3rd day.

Given 3 doses of *E. l. Blume* with lemon water.

Temperature
8 a.m. 97.8°F.
2 p.m. 98.4°F.
5 p.m. 97.0°F.

4th day.

Given 3 doses of *E. l. Blume* with lemon water.

Temperature
8 a.m. 98.0°F.
2 p.m. 98.2°F.
5 p.m. 98.0°F.

5th day.

Given 3 doses of *E. l. Blume* with lemon water.

Temperature
8 a.m. 98.2°F.
2 p.m. 98.0°F.
5 p.m. 99.0°F.

(Slide — ve.)

Patient was discharged. No relapse was reported within next 6 weeks.

PROTOCOL 3

Name	Age	Type of infection
Dal Chand	40	B.T. rings

(Temperature on admission was 104.6°F. He was given calomel at night followed by mag. sulph. early next morning.)

2nd day.

3 doses of *E. l. Blume* were given with lime water.

Temperature
8 a.m. 102.0°F.
2 p.m. 104.0°F.
5 p.m. 102.0°F.

3rd day.

3 doses of *E. l. Blume* were given with lemon water.

N.B.—Complained of nausea, extreme thirst and dryness, headache.

Temperature
8 a.m. 102.4°F.
2 p.m. 104.6°F.
8 p.m. 101.6°F.

4th day.

3 doses of *E. l. Blume* were given.

Temperature
8 a.m. 101.4°F.
2 p.m. 104.8°F.
5 p.m. 100.8°F.

5th day.

Patient restless, insomnia.

Temperature
8 a.m. 102.4°F.
2 p.m. 103.4°F.
5 p.m. 100.6°F.

Discharged as not cured.

PROTOCOL 4

Name	Age	Type of infection
Ganeshi	16	B.T. rings

(Temperature on admission was 105.0°F., was given calomel at night followed by mag. sulph. next morning.)

2nd day.

Given 3 doses of *E. l. Blume* with lemon water.

Temperature
8 a.m. 104.8°F.
2 p.m. 104.0°F.
5 p.m. 103.8°F.

3rd day.

Nausea and vomiting, extreme thirst and headache. 3 doses of *E. l. Blume* were repeated with lemon water.

Temperature
8 a.m. 103.4°F.
2 p.m. 104.0°F.
5 p.m. 104.0°F.

4th day.

Headache and nausea.

3 doses of *E. l. Blume* were given with lemon water.

Temperature
8 a.m. 103.6°F.
2 p.m. 104.6°F.
5 p.m. 104.8°F.

5th day.

3 doses of *E. l. Blume* were given with lime water.

Temperature
8 a.m. 104.0°F.
2 p.m. 104.0°F.
5 p.m. 104.2°F.

Not cured and left.

PROTOCOL 5

Name	Age	Type of infection
Rudra	17	M.T. rings

(Temperature on admission was 105.6°F., given calomel at night followed by mag. sulph. next morning.)

2nd day.

3 doses of *E. l.* Blume were given with lemon water.

Temperature
8 a.m. 100.0°F.
2 p.m. 99.0°F.
5 p.m. 99.2°F.

3rd day.

3 doses of *E. l.* Blume were given with lemon water.

Temperature
8 a.m. 99.0°F.
2 p.m. 98.2°F.
5 p.m. 98.0°F.

4th day.

3 doses of *E. l.* Blume were repeated with lemon water.

Temperature
8 a.m. 98.2°F.
2 p.m. 98.0°F.
5 p.m. 98.0°F.

5th day.

3 doses of *E. l.* Blume were given with lemon water.

Temperature
8 a.m. 97.4°F.
2 p.m. 98.4°F.
5 p.m. 98.2°F.

(Slide — ve.)

Discharged as cured, no relapse reported for 6 weeks.

PROTOCOL 6

Name	Age	Type of infection
Ganga	18	M.T. rings

(Temperature on admission was 105.4°F., given calomel at night and followed by mag. sulph. early next morning.)

2nd day.

3 doses of *E. l.* Blume were given with lemon water.

Temperature
8 a.m. 100.4°F.
2 p.m. 99.6°F.
5 p.m. 98.0°F.

3rd day.

Slight nausea and thirst.

Temperature
8 a.m. 98.6°F.
2 p.m. 98.8°F.
5 p.m. 97.8°F.

4th day.

Temperature
8 a.m. 98.0°F.
2 p.m. 98.0°F.
5 p.m. 98.0°F.

5th day.

3 doses of *E. l.* Blume were given with lemon water.

Temperature
8 a.m. 97.8°F.
2 p.m. 98.4°F.
5 p.m. 97.8°F.

(Slide — ve.)

Discharged as cured. No relapse during next 6 weeks.

An analysis of all the 32 cases indicates that out of 14 M.T. cases 68 per cent recovered and 32 per cent showed a relapse after 8 weeks, and out of 18 B.T. cases 77 per cent recovered and 33 per cent relapsed after 4 weeks. Although the number of cases tried is too small to warrant specific conclusions the percentage seems to be less than quinine. But the ill effects namely nausea, headache, ringing of ears consequent on quinine therapy were not seen.

Disadvantages.—The bitter taste and the large quantities in which the plant powder is given is not relished by children. Occasionally the patient complains of extreme thirst and drying of the tongue.

Conclusion

From the few observations made so far it may be concluded that *chhota chiraita* cannot compete with cinchona alkaloids in its effectiveness, but since quinine and other imported antimalarials are not within easy reach of every afflicted person, it is appealed to members of the medical profession to give it a trial.

Acknowledgment

The author is indebted to Dr. N. D. Kehar, M.Sc., S.C.D., Officer-in-charge, Animal Nutrition Section, Imperial Veterinary Research Institute, Izatnagar, for his valuable help and guidance in this investigation.

UNDULANT FEVER IN BOMBAY*

By L. MONTEIRO, M.D.

and

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UNDULANT fever is not confined to the small island of Malta where it was first recognized but is known to occur all over the world. It has been reported from North and South America, England (Cruikshank and Barbour, 1931; Wade, 1933), from various parts of Europe particularly Denmark; from China, the Philippine Islands, Africa and Australia. It has also been reported from various parts of India: from the Punjab (Bardhan, 1943), from South India (Pandalai and Raman, 1941), from Bengal (Chaudhuri and Rai Chaudhuri, 1943) and from Bombay (Vaidya, 1939; Joshi, 1944).

This paper is a summary of proved cases of the disease admitted to the various hospitals of Bombay and studied in the course of the last three years.

Age and sex.—In this series of nine cases the youngest was a girl of 11 and the oldest a man aged 60 years, the rest ranging from 18 to 42 years which is the susceptible age period for undulant fever. Six were males and the rest females.

Occupation.—Occupation plays a definite rôle in the ætiology of the disease because of the opportunities it provides for infection. Of the nine cases one was a cleaner of hides in a tanning factory, one a butcher, one a salesman in a milk shop and one attended a ewe during an abortion. In the rest the nature of their occupation did not seem responsible for the infection.

Three cases (nos. II, VII and IX) contracted the infection through skin contact and one case (no. VIII) by drinking the milk of a ewe which had aborted. In the rest of the cases the infection was presumably conveyed through milk taken raw. Cases nos. VIII and IX are examples

* A paper read before the meeting of the Association of Physicians of India held in Bombay in April 1946.

of infection occurring in the same family the first by drinking raw milk and the other by skin contact.

As regards the communal incidence six were Hindus, two Muslims and one Christian.

Residence.—Five out of the nine cases came from Kathiawar and Cutch (Western India). The cases reported by Vaidya (1939) and the one of Joshi (1944) were also from Kathiawar. It would seem that brucellosis is quite prevalent in Kathiawar. Cases nos. I, II and VII came from the suburbs of Bombay.

conclusion can, however, be arrived at only by a bacteriological examination.

In the present series, the diagnosis was made when the fever had lasted for more than two months. Till then, the investigations and treatment postulated malaria, typhoid or tuberculosis. Only when the fever failed to respond to anti-malarial drugs, and laboratory examinations for the enteric group of organisms and tuberculosis were negative, was the possibility of undulant fever envisaged. The first investigation that pointed the nature of the disease was the

TABLE I

Case number	Age	Sex	Religion	Place	Mode of infection	Month
I	42	M.	Ch.	Bandra (Bombay)	Hog contact milk	October
II	18	M.	H.	Bombay	Tanner (contact)	April
III	26	M.	H.	Nasik	Milkman	October
IV	11	F.	M.	Kathiawar	Milk	January
V	36	M.	H.	"	"	October
VI	30	F.	H.	"	"	November
VII	40	M.	M.	Kurla (Bombay)	Bitcher	September
VIII	60	M.	H.	Cutch	Milk	November
IX	30	F.	H.	"	Contact	August

Seasonal incidence.—Seven cases out of nine started getting fever between the months of August and November (table I). Case no. II (the tanner) contracted the fever in April and no. IV in January. This August to November period is noteworthy, as it is the calving season for cattle in India generally and the period of increased production of milk. The contamination of the milk with brucella organisms will therefore be more marked during this season. In various other countries where undulant fever is prevalent, the highest incidence coincides with the calving or kidding season, the season in which large quantities of milk are produced.

Clinical symptoms and signs.—Prolonged continuous fever was the main symptom in all the cases. In the majority of them, the fever was continuous in the first month and the undulations became evident in the third month of the disease. The longest duration was twelve months and the shortest three months. Loss of weight occurred in five out of nine cases; it was marked in three cases. In spite of the high fever persisting for months the patient hardly looked ill and two of them continued to do light work. Chills occurred in four cases and two of them complained of profuse perspiration. There were few physical signs. The spleen was palpable in five cases and there was bronchitis in two cases. The liver was palpable in two cases. Arthritis and rheumatic pains in the joints were present in cases nos. II, VI, VII, VIII and IX.

Laboratory diagnosis.—A clinical diagnosis of brucellosis is no easy problem in view of the occurrence of atypical and subclinical infections. If this condition is kept in mind, especially in cases of pyrexia of obscure origin, a larger number of cases may come to light. A definite

agglutination test. This, as mentioned before, was carried out well-nigh two months after the onset of the disease, at a time when the agglutinins in the blood would be present in a suggestive titre. The test was carried out against standard Oxford suspensions of *B. abortus* and *B. melitensis*. The highest titres obtained varied from about 1 in 500 to 1 in 3,500. In some cases differentiation as to the type of infection could not be arrived at from these results. Table II shows the various titres obtained. Agglutinin absorption tests with serum obtained from patients were not carried out. Such high titres are rarely met with, except as a result of active infection, and in clinically suspected cases is strong evidence in favour of brucellosis. In two cases where the blood culture was negative the diagnosis depended on the agglutination test alone. It must be emphasized that a negative agglutination reaction is possible even during the active phases of the disease and for a comprehensive study the isolation of the causative organism becomes imperative.

The organism can be isolated most frequently from the blood. Blood culture was carried out in all the cases. As will be seen from table II organisms belonging to the genus *Brucella* were grown in seven cases out of the total of nine. The blood was collected at the height of the fever, if present, or after a provocative milk injection. Ten ml. of blood were inoculated in Hartley's broth and incubated under ordinary atmospheric conditions. Growth was observed about a week later, subculture being made on nutrient agar and the morphological and cultural characters studied. Biochemical reactions showed no fermentative activity with the usual carbohydrate

TABLE II

Case number	AGGLUTINATION TITRE OF SERUM AGAINST STANDARD SUSPENSIONS		Blood culture	H ₂ S	ANTIGENIC STRUCTURE MONO-SPECIFIC OXFORD SERA		Classification of organism
	<i>Br. melitensis</i>	<i>Br. abortus</i>			<i>Br. abortus</i>	<i>Br. melitensis</i>	
I	Not done	500	Positive	+ ve	25 complete	25 complete	Probably <i>Br. abortus</i> .
II	"	2,000	"	+ ve	50 incomplete	50 incomplete	
III	"	500	"	"	100 complete	50 complete	
IV	2,000	1,000	No growth	..	200 incomplete	100 incomplete	<i>Br. abortus</i> .
V	"	1,000	Positive	+ ve	50 complete	50 complete	
VI	2,000	1,500	No growth	..	100 incomplete	100 incomplete	Probably <i>Br. abortus</i> .
VII	2,000	2,000	Positive	- ve	125	50	<i>Br. melitensis</i> ?
VIII	400	400	"	+ ve	125	50	<i>Br. abortus</i> .
IX	2,000	3,500	"	- ve	125	25	<i>Br. abortus</i> ?
	1,000	2,000	"	- ve	50 complete	25	<i>Br. abortus</i> ?
	500	1,000	"	- ve	125 incomplete		

substrates. The production of hydrogen sulphide (H₂S) was observed for at least seven days. The organisms were tested against mono-specific Oxford sera. Table II shows the results. All the serological reactions were carried out soon after the isolation of the organism, in their smooth phase, before a change of the antigenic structure to a rough form could occur.

The classification and identification of these organisms is difficult because of the subtypes of the related types. The criteria usually used in the differentiation of the various types are the CO₂ sensitivity at primary isolation, growth in the presence of dyes, H₂S elimination, the antigenic structure and the virulence test. All the strains in the present series were isolated after incubation in air without an increased CO₂ tension. It was observed that the growth in the primary cultures was slow, taking a week or more to appear. It is conceivable that the small amount of CO₂ present after inoculation of the medium and the burning of the plug was sufficient to initiate the growth, the CO₂ requirements subsequently being supplied by the growing organisms themselves.

Cultivation in the presence of dyes to test their inhibitory activity gave equivocal results and was not persisted with. Inability to obtain the standard dyes may have been responsible for these results. Virulence tests were not attempted in any of the cases.

An analysis of table II reveals several interesting features. It will be seen that, out of the total of seven strains, only two can definitely be placed as *Brucella abortus* (cases nos. II and VII). Cases nos. I and IV showed cultural characters of *Br. abortus*, though antigenically the results were not conclusive. Case no. VI, though culturally resembled *Br. melitensis*, antigenically belongs more to the *abortus* variety. Cases nos. VII and VIII, where contact has been with sheep, antigenically resemble

Br. abortus, though H₂S was not produced. These results have been very confusing, but as mentioned at the beginning of this section, the existence of subtypes is probably responsible for this state of affairs.

Not all varieties of *Brucella abortus* require the presence of increased CO₂ tension during primary isolation. The Southern Rhodesian variety (Topley and Wilson, 1946) is an example. Again there have been strains isolated in S. E. France (Topley and Wilson, 1946) which, though they show the biochemical characters of *Br. melitensis*, possess the antigenic structure of *Br. abortus*.

The animal source of origin may be extremely helpful, especially as the above investigations are not very conclusive. Polding (personal communication, 1946) working on brucellosis, at the Imperial Veterinary Research Institute, Mukteswar, India, finds in a total of 49 strains studied, 26 *Brucella abortus*, 3 *Br. melitensis* and 20 unclassified strains. Of the three *melitensis* strains, one was obtained from a cow, one from a goat and one from a human source. The rest of the strains were all obtained from cows, buffaloes and one from a horse. The unclassified strains gave ambiguous results, among other characters the ability to grow in air at first isolation, the production of H₂S, and antigenic instability. The larger number in his series were *abortus* and the smaller number *melitensis*, serological differentiation not being as sharp as in the standard strains. This unclassified group has been called the aberrant variety and is indigenous to this country.

The doubtful strains in our series, therefore, could correspond to the aberrant variety described by Polding or to some other subtype. A fuller investigation on a larger number of strains should throw some light on the occurrence of indigenous variants in this country.

The third type of brucella organism, *Br. suis*, responsible for some cases of the disease in

America and Denmark, antigenically and biochemically related to *Br. abortus*, cannot be differentiated from this organism. The dye tests, the animal source and the country of origin are useful. No cases of infection by *Br. suis* have so far been reported from India. In the present series, there is one case in which there has been contact with hogs (case no. I), where the infecting organism is probably *Br. abortus*.

It is well known that the three main types, *Br. melitensis*, *Br. abortus* and *Br. suis* produce the disease in goats and sheep, cattle, and hogs respectively. Interchangeability of the host is known to occur either as a result of contact or under experimental conditions. The occurrence of *Brucella abortus* type of organism in sheep (cases nos. VII and VIII) may, therefore, be accountable.

In India, several workers have reported cases of brucellosis. In some of these cases, the ætiological agent has been isolated. This has in every instance been *Br. melitensis*, a contrast to the present series.

Treatment.—Most of our cases were treated symptomatically before the diagnosis was established and all of them unsuccessfully with quinine and mepacrine in the early stages. When the fever still persisted, they were treated as enteric infections. Once the diagnosis of undulant fever was proved an adequate diet was given. This series was treated with sulphonamides. This was completely successful in three cases and curtailed the length of bouts in others. In case no. I sulphaguanidine was given continuously in a dosage of 8 gm. a day for ten days. The fever settled down on the fourth day and remained normal afterwards. After an interval of seven days sulphaguanidine was repeated in the same dosage for eight days. The fever never recurred. In cases nos. VIII and IX sulphadiazine in a daily dosage of 4 gm. brought the temperature down to normal on the sixth day and has remained normal since then. Sulphadiazine was given in these cases consecutively for eighteen days. In case no. VII, 9 gm. of sulphamerazine was given daily for 18 days, i.e. a total of 187 gm. The temperature settled down to normal on the sixth day and remained so for one month. There was a relapse and consequent readmission during which period the organism was again isolated from the blood. Sulphamerazine was again successful in curtailing the relapse. In cases where sulphonamides were administered, blood was frequently examined to check its level and the effect on the cytological element. Bardhan (1943) reported the curative effect of the drug in cases which he treated in Lahore. Debono (1939) on the other hand pronounced them ineffective in a series of 25 cases of undulant fever in Malta. Horn (1940) found them exercising a favourable influence on the subjective symptoms of the disease. On a review of literature available and from personal experience of the above cases it

can be reasonably concluded that sulphonamides are not specific in the treatment of undulant fever. They do however abort the bouts of fever and thus shorten the period of relapse undulation. Chaudhuri and Rai Chaudhuri (1943) came to similar conclusions. Other drugs were not tried in this series.

Mode of infection and infecting organism.—In case no. II (tanner) and case no. VII (butcher) the infection was obviously contracted through the skin while handling a brucella infected carcass or meat. Case no. IX got infected through handling the afterbirth of the ewe which had aborted and case no. VIII by drinking raw infected milk of the same animal. In both of these cases the infecting organism was probably *Br. abortus*. It is known that sheep carry *Br. abortus* infection. The remaining four cases (three from Kathiawar and one from Nasik) probably developed infection by drinking raw milk of cattle or sheep. In the fourth the organism was not isolated. In the case from Bandra (case no. I) the source of infection could not be ascertained but was probably with milk or contact with hog.

The type of organism.—*Br. abortus* or its aberrant varieties were isolated from six out of seven positive cultures. This fact suggests cattle (cow and buffalo) rather than goat to be the source of infection. Cattle in India are known to carry *Br. abortus* infection and so also may Indian sheep by contact with infected cattle. In parts of America where cattle breeding is common *Br. abortus* infection is more predominant than *Br. melitensis*. In England, too, *Br. abortus* is much commoner than *Br. melitensis* infection, so much so that 95 per cent of undulant fever there is ascribable to *Br. abortus*. Out of 49 strains of *Brucella* studied at Mukteswar the majority were of *Br. abortus* variety or its Indian aberrant types. In India only a negligible quantity of goat's milk is consumed and that too only by shepherds. Milk in general use is from the buffalo, the cow and to a slight extent from the sheep. In certain parts of the country raw milk is habitually drunk from a common belief that raw milk is more nutritive. A possible source of infection may thus be the milk from infected cattle and conceivably undulant fever may be more widespread in our country than is generally realized. This is probably even more true for the rural than the urban areas.

Kristensen (1928), commenting on the high incidence of *Brucella abortus* infection among the population of Denmark, stated 'there is no reason to believe that this infection is more widespread here in Denmark than in other countries where cattle breeding is carried on to some extent. It must be supposed that if systematic inquiries of a similar nature were set on foot in Germany and England the same condition would be found'. India owns one-third of the cattle of the world, and there is no reason why Kristensen's remarks should not apply

to this country. By co-operation between physicians, veterinary surgeons and public health (milk) authorities, the sources and prevalence of infection would, it is suggested, be probably detected earlier.

Summary

1. Nine cases of undulant fever are reported. Seven diagnosed by isolation of the organism and two by agglutination test.
2. The source and mode of infection of these cases are discussed.
3. The treatment of undulant fever with sulphonamides is described. The results are not encouraging.

We thank the Dean and the Physicians of K. E. M. Hospital for allowing us to investigate, treat and report some of the cases. Dr. B. M. Amin was responsible for the isolation of the first two strains. We also thank Drs. B. B. Yodh, M. J. Shah and Jhatakia of Sir H. N. Hospital, and Dr. A. Karamally of Habib Hospital, for permitting us to study their cases. Our thanks are due to Dr. R. Row, Director, P. G. Singhanee Hindu Hospital, for allowing us to publish the notes of the last two cases. We are grateful to Dr. C. G. Pandit, Guindy, for his study of the first three strains.

Appendix of Case Notes

Case no. I.—M. R., male, 42, Christian, clerk by occupation, residing in Bandra (Bombay Suburban District), was having a continuous temperature for nearly 2 months when he was first seen by one of us (J. C. P.) at his residence. There were no physical signs except that he was emaciated and anæmic. The usual investigations like urine, stool and Widal tests were negative. The total and differential leucocytic counts were normal. He was treated as a case of enteric fever even though the serology was negative. He was allowed a more liberal diet than he hitherto had, but the temperature continued for another month. He was admitted to the K. E. M. Hospital for investigation on 15th December, 1943. On admission there were no physical signs except loss of weight and anæmia. The spleen was not palpable. Total W.B.C.s 8,400 per c.mm., the differential leucocyte count was neutrophils 62 per cent, eosinophils 3 per cent, lymphocytes 33 per cent, monocytes 2 per cent; Kahn and Widal tests were negative. Skiagram of the chest was normal. Blood agglutination against *Br. abortus* was positive 1 in 500. Organisms of brucella group, probably *Br. abortus*, was grown from the blood. His temperature settled down and he left the hospital on 30th December, 1943. A recurrence of the fever after an afebrile period of 8 days brought him back to the hospital. Blood agglutination showed a higher titre (1 in 2,000) and the same organism was grown again from the blood. He was treated with sulphaguanidine in the dosage of 2 gm. three times a day for 15 days and it was repeated after an interval of 8 days. There was no recurrence of the fever, and convalescence was uneventful.

There was no contact with any animal except hogs, and the milk consumed by him was from the cow and the buffalo.

Case no. II.—M. S., male, aged 18, Hindu, living in Dharavi (Bombay Suburban District) and employed in a tannery for cleaning hides, was admitted in the K. E. M. Hospital on 27th July, 1944, with a history of continuous fever for 8 days. He had irregular fever for 6 weeks in the hospital and his Widal reaction carried out at intervals of 15 days was thrice negative. There were signs of bronchitis in the chest and the spleen was palpable. The total and differential leucocytic count was within normal limits. On 30th September, 1944, blood agglutination against *Br. abortus* was positive 1 in 5,000 and on 10th October, 1944, increased to 1 in 1,000. Agglutination titre even though examined twice later remained the same. Blood culture taken on 10th October, 1944, grew *Br. abortus*. He was treated with sulphathiazole which brought the temperature to normal and the patient left the hospital against medical advice. Subsequently he came to the out-patient department and complained of pain in the joints. His knee, ankle and shoulder joints were swollen and painful for about 8 days. He had two further bouts of fever each lasting for 8 days for which he did not take any treatment.

Case no. VIII.—H. H., 60, Hindu male, was admitted in the P. G. Singhanee Hindu Hospital on 11th December, 1945, with a history of irregular fever and dry cough of one month's duration in Cutch. Physical examination showed enlargement of the spleen, one finger breadth below the costal margin and rhonchi with prolonged expiration in the chest. The patient was a subject of bronchial asthma. The fever occurred usually in the afternoon without rigors. The patient enjoyed a good appetite. All routine investigations were negative. The temperature did not respond to quinine and atabrin, serum agglutination test was positive for *Br. abortus* and *Br. melitensis*, 1 in 1,000. A blood culture taken on 10th January, 1946, was positive. He was treated with sulphadiazine 4 gm. a day. The temperature settled to normal on sixth day of the treatment. He was discharged on the eleventh day with instructions to continue the drug which he did for about 7 days and discontinued of his own accord. There had been no recurrence of the symptoms till July 1946.

Case no. IX.—A Hindu female, aged 30 years, the daughter-in-law of case no. VIII, was admitted to the P. G. Singhanee Hindu Hospital on 11th December, 1945, with a history of irregular fever for 4 months, cough 2 months and pain in the right side of the chest for 2 months. The fever rose occasionally to 104°F. and was accompanied by chills. On examination there were no physical signs detected except that the patient was pale and anæmic. The usual investigations, including a total and differential count, Widal reaction, urine analysis.

and culture, stool, gastric analysis and a fluoroscopy of the chest were negative. Agglutination of the blood carried out on 27th December, 1945, was positive for *Br. abortus* 1 in 1,000 and *Br. melitensis* 1 in 500. A culture of the blood was positive for *Br. abortus* (?). The treatment consisted of sulphadiazine 4 gm. a day for 18 days. There had been no relapse till July 1946.

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CERVICAL RIB SYNDROME

WITH A CASE RECORD

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CERVICAL ribs in man are anomalous structures rather than examples of evolution or reversion. The embryological formation of supernumerary ribs is attributed to a conflict between forming plexuses and ribs. In high forms the limb buds cover several vertebral segments, the nerves from which grow into the buds. The nerves have to follow an oblique course before entering the buds due to a different pace of growth between the column and the buds. The obliquely running nerves impede the growth of the ribs to the extent that they merely form vertebral processes.

Anatomical classification.—Cervical ribs are divided into four groups according to the extent of growth.

1. Slight degree—the rib reaching just beyond the transverse process.
2. More advanced—the rib touches the first rib.
3. Almost complete—the rib connecting with the cartilage of the first rib.
4. Complete—the rib possessed of a true cartilage and articulating with the cartilage of the first rib.

Incidence.—In a review of cases observed at the Mayo Clinics the incidence was 0.056 per cent. It was more common in females than in males, a ratio of 2.5 to 1. Bilateral ribs were present in almost half the cases and unilateral ribs were equally frequent on either side. In a little over half the cases the cervical rib was

discovered accidentally. Age incidence is usually from 25 to 30 years.

Symptoms and signs.—In a large group of cases the symptoms are referred to the lower trunks of the brachial plexus, and consist of pain referred to one of the nerves. The pain is worse after exertion, and is invariably exaggerated by the rotation of the head or forceful downward pull of the shoulder. Atrophy of the intrinsic muscles of the hand is a late phenomenon, and may affect the distribution of the median and ulnar nerves. Hyperæsthesia, paræsthesia and anæsthesia may also be present along with pain.

Circulatory symptoms are rarely severe, one hand or arm sometimes more deeply cyanotic than its opposite number. Mild trophic changes in one or more finger tips or even gangrene of one or more fingers may be seen. Diminution in the volume of radial pulse is common, the pulse can be decreased or stopped by making the patient elevate the chin and rotate the head to the affected side. This movement also affects blood pressure readings on the affected side. These symptoms are produced as a result of pressure on the subclavian artery which is squeezed with the brachial plexus between the cervical rib and the lateral border of scalenus anticus muscle.

One or the other types of symptoms may predominate. The writer has successfully treated three patients who complained of pain by partial excision of the rib. The present case is of interest in that it presented only mild vascular symptoms and was successfully treated by division of the scalenus anticus muscle on the affected side. In the former cases the rib was almost complete in nature, and in the case under review it was only rudimentary.

Case Notes

A Hindu male, aged 20 years, service 3 years, a heavy manual worker, first reported sick in January 1946 for painful swelling over the left shin bone, and was admitted to a C. C. S. This was treated with fomentations and subsided in 12 days and the patient was discharged to duty. He was readmitted after two months for a similar complaint on the right side, and in addition he had a painful swelling on the tip of the left middle finger. The former resolved in ten days while the latter burst and a small amount of sero-purulent discharge came out. W. R. and Kahn tests were negative. There were no other complaints. He was transferred to this hospital in May 1946 as a case of ? thrombo-angiitis obliterans. On admission the following facts were elicited. The patient was perfectly well up to four months ago. He had never experienced any pain or cramps in the legs and denied history of venereal disease.

Physical examination.—A small gangrenous patch was seen over the palmar aspect of the tip of the left middle finger. The left hand and forearm were definitely cold compared to the right side. No pulsations could be felt in the

radial or ulnar arteries in the forearm. A very feeble pulse could be felt at the bend of the elbow. No neurological signs were discovered, and there was no atrophy of the intrinsic muscles of the hand. There was no evidence of circulatory disturbance in the lower limbs.

Blood pressure readings on the right side : 110/75 mm. Hg. On the left side : 90 mm. systolic, diastolic could not be recorded.

Blood pressure reading on the left side with chin elevated and head rotated to the affected side : 70 mm. systolic.

X-ray examination of the neck revealed bilateral cervical ribs. The one on the right side was well developed and quite prominent on the radiogram, whereas the one on the left was rudimentary and formed an acute angle at its junction with 7th cervical transverse process (see figure, plate XXXI). The terminal phalanx of the left middle finger was normal in appearance.

Operation notes (13th May, 1946).—General anaesthesia was induced with ether and oxygen after premedication with morphia and hyoscine. The posterior triangle was opened through an oblique incision about 4 inches in length, starting just near the sterno-clavicular junction and extending backwards with slight inclination upwards. The clavicular portion of the sternomastoid was divided between clamps. The phrenic nerve running obliquely downwards and inwards over the scalenus anticus was identified and retracted medially. The transverse cervical artery was divided between clamps and ligated. The insertion of the scalenus anticus to the first rib was exposed and the trunks of the brachial plexus identified. No visible pulsation was noticed in the third part of the subclavian artery, but on palpation a feeble pulsation could be felt. The scalenus anticus was divided piecemeal near its insertion starting from the outer edge. The most remarkable thing noticed after the division had been completed was the forceful pulsation in the subclavian artery distal to the muscle. The wound was closed after restoring the continuity of the sternomastoid muscle.

Post-operative observation.—1. Immediately after operation : The brachial artery at the bend of the elbow could be very easily felt and the force of pulsation had definitely increased. No pulsation was felt either in the radial or ulnar arteries.

2. Forty-eight hours later : Good pulsation could be felt in the ulnar artery in its upper two-third; no pulse in the radial. Blood pressure on the affected side 95/75 mm. Hg. The hand was distinctly warmer than before.

3. One week later : Blood pressure equal on both sides, no radial pulse (? obliterated vessel). Gangrenous patch showed signs of separation.

A fortnight after the operation the patient was up and about and had full use of his left hand.

In the absence of an arteriogram it is assumed that the radial artery was either abnormal in its course or had been obliterated.

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IS SECOND ATTACK OF DIPHTHERIA POSSIBLE ?

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So far as the production of immunity is concerned infectious diseases may be broadly divided into three groups. In the first of these are the diseases which invariably kill the organism as the infection is so severe and virulent that it produces a complete breakdown of the immunity mechanism of the victim. Hydrophobia and bacterial endocarditis are some of the common examples belonging to this category. In the second group there are diseased conditions in which the first attack predisposes the victim to further attacks. Here, as a result of infection, the immunological response of the patient is such that either he gets a short-lived immunity after the expiry of which he cannot ward off a second attack, or the infection instead of producing any strong immunity makes the organism more susceptible to the infection or, in other words, it gives rise to bacterial allergy. Pneumonia, tuberculosis, rheumatic fever and influenza are some of the common examples of this group. In the third are included all those infections in which one attack produces a life-long or at least a fairly prolonged immunity in the organism so that he seldom suffers from a second attack subsequently. Here the immunological response of the animal is so strong and lasting that he can ward off a second attack even after a long time has elapsed since the first. Typhoid fever, small-pox and diphtheria are some of the examples of this group.

Infants do not suffer from diphtheria as they imbibe sufficient immunity from the mother through the placental circulation. But as the baby gets older, this immunity which is of the nature of passive immunity rapidly disappears and his susceptibility to infection now becomes marked. This is the reason why a child after the age of one year often suffers from diphtheria. During an attack of the disease, the toxin is absorbed into the blood and stimulates the tissues of the body to form immune bodies against it but mobilization of the defensive

forces cannot keep pace with the manufacture of the toxin at the site of infection which therefore gets the upper hand and kills the patient by serious damage to his vital organs. During treatment which is usually started after some toxin has already entered the circulation, the excessive amount of the poison is neutralized by the antitoxic serum which thus saves the vital organs from damage whilst some quantity of toxin which had already entered the circulation before the antitoxin treatment was started serves as the vaccinating dose to produce an active immunity. It is admitted by everybody that the best way to develop a lasting immunity is to suffer from an attack of the disease. Thus one attack of clinical diphtheria usually gives a life-long immunity and we do not find the occurrence of a second attack of diphtheria even after a long time has elapsed since the attack of the disease. Even active immunity induced artificially by injection of modified toxin lasts at least for one year. The writers have met with an instance in which a child suffered from two severe attacks of diphtheria within a period of 9 months.

Case Notes

M. M., a Muslim male child, aged 1½ years, was admitted into the Medical College Hospital on 27th May, 1946, with a history of fever for five days with slight dry cough. For the past 3 days the child was having difficulty in breathing with hoarseness of voice. He was also getting pain in the throat and difficulty in swallowing.

Past history.—About 9 months back, the child had suffered from a severe attack of diphtheria. At that time the throat swab was positive and he received in all 110,000 units of antitoxin. He got well, and since then was keeping fit.

On examination.—The child looked well built and well nourished. Slight suction was present. No cyanosis. Tonsils were moderately enlarged, looked inflamed and revealed moderate-sized patches on both. Lungs showed poor air entry and a few râles at the bases. Heart showed no abnormality. Liver and spleen not enlarged. No abnormality detected in the nervous system. Temperature 101.5°F., P/R 170/48, pulse poor volume and low tension. Anti-diphtheritic serum 60,000 units was injected intramuscularly *stat*, and penicillin 10,000 units intramuscularly every 3 hours was started.

Progress of the case.—As the suction increased, tracheotomy had to be performed for relief in the night. On the next day 40,000 units of antitoxin were injected intramuscularly, and penicillin in doses of 15,000 units every 3 hours intramuscularly was continued. Two days later, a membrane 3 inches long came out of the tracheotomy tube and after this incident breathing improved. As the patch in the throat did not disappear completely another quantity of 30,000 units of anti-diphtheritic serum was

given intramuscularly, the penicillin injection being continued. On 1st June, the throat became clear and a day later, the throat and tracheal swabs became negative. Penicillin was stopped on 3rd June, when altogether 640,000 units were administered. The child subsequently made an uneventful recovery, and he was discharged from the hospital on 10th July.

Comments

The case described above is of considerable scientific interest as the child had two severe attacks of diphtheria within a comparatively short period of 9 months. The writers have not seen any reference to such cases in the recent literature and no such case was admitted into the Medical College Hospital during the last 20 years. Though virulence of the cultured organisms was not tested, their morphological characters, the clinical course of the illness and the response to anti-diphtheritic serum indicated that both these attacks were due to a virulent type of *C. diphtheria*. The child should have developed a strong immunity after the first attack but prior to his second illness his immunological defences against diphtheria must have broken down to such an extent as to make him susceptible to the disease again. What this adverse factor might have been, we do not know. His general health previous to the present attack was quite good and there was no abnormality except moderately enlarged tonsils. Or is it possible that the child failed to develop any active immunity for some unknown reason but the large quantity of anti-diphtheritic serum was able to cure the disease? A Schick test done on such a case might have been of great help to ascertain this point. Unfortunately no information in that direction was available as the child was treated at home by a private doctor in consultation with a medical specialist. Besides, there was no suggestion that a Schick test was indicated as the child made a usual recovery without any complication.

The writers acknowledge the help from the Professor of Pathology, for his bacteriological reports. They are also indebted to the Superintendent, Medical College Hospital, for his permission to use the records of the hospital.

TROPICAL EOSINOPHILIA

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I. Introduction

THE rôle of the eosinophil cell in the immunity mechanism of the body is not yet fully understood. It is however well known that an increase of eosinophil cells is produced and maintained by a variety of parasitic infections as well as in certain diseases whose aetiology has hitherto been undetermined. But massive eosinophilia, considerably in excess of that noted in these infections, has been recorded from time to time in tropical subjects

and on apparently tenable grounds, a new disease tropical eosinophilia has been reckoned. In 1938, this was considered a distinct clinical entity by Saint Etienne but the complete clinical syndrome was first described by Frimodt-Møller and Barton in 1940. They described cases of eosinophilia associated with radiological changes in the lungs which differ from Loeffler's syndrome and having no connection with tuberculosis. Weingarten (1943) described 81 cases of massive eosinophilia with pulmonary symptoms in persons belonging to different communities from the western coast of India. He called the condition 'tropical eosinophilia' and adduced evidence to justify its recognition as a disease entity, apparently peculiar to certain parts of India. He gave a clearer clinical picture and stated arsenic to be a specific remedy. Similar cases have been reported by Treu (1943), Simeons (1943), Owen (1943), Heilig and Visveswar (1943), Vaidya (1943), Patel (1943), Parsons-Smith (1944), Chaudhuri (1943), Roy and Chakravarty (1943), Shah (1943), Emerson (1944), Carter, Wedd and d'Abnera (1944) and Soysa and Jayawardena (1945).

This article is the result of detailed analytical study of 16 cases of massive eosinophilia that had been under the care of the writer from 1943 to 1945. These cases had sought medical advice on the suspicion of tuberculous affection or asthma and had treatment in the tuberculosis clinic under the supervision of the writer. They constituted 5 per cent of the total admissions to the tuberculosis clinic.

II. Analysis of Cases

(a) *Geographical distribution.*—All the cases studied are from coastal towns and villages of Kathiawar. Since most of the cases attending the 'T. B. Clinic' under the writer's care are also from the same locality, it cannot be definitely asserted that there is greater incidence of the disease in the coastal areas as observed by many other writers on the subject. Weingarten has observed that most of his cases were persons living near the sea. He has seen very few cases among those who lived inland. He reported one case from the United Provinces of a girl who lived for some time in swampy area. Most of the cases reported by others are also from coastal areas of India. The influence of environment as an ætiological factor is considerable.

(b) *Sex.*—Out of 16 cases studied 10 were males and 6 were females. Analysis of tuberculous patients admitted to the clinic during the same period showed that 70 per cent were females and 30 per cent males. This is a noteworthy observation, since although a higher incidence of tuberculosis is seen in the purdah-observing Muslim women of Kathiawar, the incidence of eosinophilia is seen to be less than in the cases of males. Treu (1944) made the observation that females are less prone

to this disease. Patel (1945) reported 49 cases from Bombay of which 37 were males. He however attributed the higher number of male patients to a large proportion of males seeking medical advice or leading a more exposed life.

(c) *Age.*—The youngest patient in the series was 8 years old, and the oldest 55 years old. The largest incidence is noted in youth and early adult life. In Weingarten's series, the highest incidence was in the age group 15 to 45.

(d) *Caste.*—Only 2 cases were Hindus and the remaining 14 were Mohammedans. The same proportion was however seen more or less in the tuberculous patients admitted to our clinic and hence this factor does not seem to have any bearing on the ætiology of the condition. The disease is recognized in all communities and races in India and even in Europeans, Americans, Arabs and others.

(e) *Season.*—Seasonal variations do not seem to have any significant rôle in the ætiology of the disease although in chronic cases asthmatic attacks are precipitated by exposure to cold, winds and during monsoons.

(f) *Occupation.*—Economic conditions, smoking, addiction to alcohol, social status and food habits did not appear to have any importance in the incidence of this condition.

(g) *Allergy.*—It is often difficult to get reliable family history of allergy or constitutional susceptibility in patients. However, it was possible to establish history of allergic syndromes in the family in 4 cases. Three of the cases gave a history of asthma in the family while the fourth gave a history of migraine, epilepsy and Ménière's syndrome in the family. It is noteworthy that 2 of these cases gave strong positive reaction to intradermal histamine test while the other 2 gave doubtfully positive reactions. Weingarten stated that there was no familial or constitutional susceptibility and more than one case was not observed by him in one family, however large. The present series of cases however shows that about 25 per cent of cases gave a family history of allergy. Some observers like Patel (1945) believe that constitutional susceptibility is a significant factor in a considerable proportion of cases.

III. Clinical Picture

The clinical picture is more or less characteristic in most cases except for minor variations. As a rule the mode of onset was slow and insidious. The cases under review presented the following symptoms:—

(a) *Cough* is the prominent and invariable symptom noted in all cases and in most cases it is the most distressing symptom from which the patient desires early relief. The cough in the early stage is dry, hacking, and ineffective. Later on, it becomes paroxysmal and worse at night especially in the early hours of the morning. Some of the cases experience absolute

freedom from cough during day time. The irritable cough is often sensitive to weather, a decrease in temperature or increase in humidity causing an exacerbation. The cough was frequently unproductive, particularly in the early stages. Free expectoration was seen in 6 cases. In the beginning the sputum is glairy and tenacious while later on it becomes thin and copious. The sputum never becomes purulent or offensive in odour. Rusty or 'prune-juice' type of sputum was never observed. However, with paroxysms of cough, blood-streaking of sputum is occasionally seen and small amount of blood may be expectorated. Frank hæmoptysis was recorded in 2 cases. The bouts of cough in some patients, particularly children, ended with vomiting.

(b) *Expiratory dyspnoea*.—The paroxysms of cough sooner or later became more frequent, followed by wheezing and expiratory dyspnoea. In some cases attacks closely resembling bronchial asthma occurred regularly some time in midnight or in the early hours of the morning. If the case is pyrexial, an increase of temperature was usually noted with the paroxysms of dyspnoea. In the morning the patient feels better and comparatively relieved of his dyspnoea. Such cases therefore are naturally mistaken for bronchial asthma. A condition of status asthmaticus is rarely encountered.

(c) *Pyrexia*.—Out of 16 cases studied 11 had pyrexial reaction of some type or other and fever was one of the chief complaints. Remaining 5 cases remained practically apyrexial or with very negligible febrile upsets. The pyrexia in most cases remained more or less continuous and of the low type ranging from 99° to 101°F. Occasionally a relapsing type of fever is noted. Sharp rise of temperature up to 104° or 105°F. and persisting for a day or two is not infrequently seen in the course of the disease, particularly following the first one or two injections of arsenic. An intermittent type of pyrexia is also not unusual. This may be mistaken for malaria particularly in view of the associated splenomegaly. Profuse perspiration with the fall of temperature as is often encountered in malarial attacks is rarely seen in this syndrome.

(d) *Loss of weight*.—This is usually complained of from the beginning of the disease. The appetite is usually poor, and as a result of paroxysms of cough and dyspnoea excited by the evening meal, the patient becomes afraid of eating. The loss of weight therefore becomes considerable and in children with diarrhoea emaciation is a prominent feature.

(e) *Pain in the chest*.—Prominent among the symptoms of adult subjects of the disease is pain in the chest, usually substernal but occasionally generalized. The pain is usually of a dull aching character, but a sense of constriction is occasionally complained. Curiously enough children did not complain of any distressing pain in the chest.

When the disease shows its occasional exacerbation with sharp rise of temperature exaggeration of chest pain is also noted.

(f) *Gastro-intestinal symptoms*.—Earlier writers have not alluded to the occurrence of gastro-intestinal symptoms in this syndrome. Patel (1945) has however referred to attacks of vomiting, following a paroxysm of cough and dyspnoea. But in the series of cases studied, it has been found that gastro-intestinal symptoms were present in 3 out of the 16 cases. Children and young adults were particularly prone to exhibit gastro-intestinal disturbances. Attacks of vomiting and diarrhoea became worse with the natural exacerbations of the disease. These symptoms could not be permanently controlled by any remedy other than arsenicals. Chronic diarrhoea in these subjects was completely relieved by the arsenical treatment.

(g) *Cutaneous manifestations*.—These manifestations which had not been recorded by earlier writers on 'tropical eosinophilia' have been recognized in 4 out of 16 cases studied. The cutaneous reactions were of three types: (1) Lesions simulating erythema nodosum and erythema induratum. (2) Papular urticarial lesions. (3) Eruptions not unlike papular tuberculides. It is possible that these lesions were consequent on epidermal sensitization due to an undetected tuberculous focus somewhere in the body but the Mantoux test was positive only in 2 cases. Moreover, specific therapy with arsenicals had produced complete disappearance of the lesions without recurrence. It is therefore probable that these are specific lesions connected directly or indirectly with the ætiology of eosinophilic syndrome.

IV. Physical Signs

There was some variation of physical signs from case to case but the following are the general signs seen in the cases studied.

(a) *Bronchospasm*.—Most of the cases showed obvious evidence of bronchospasm and bronchitis-hyperresonance of the chest, prolonged expiration with sibilant and sonorous rhonchi all over the chest. Old subjects of the disease show evidence of emphysematous changes in the chest.

(b) *Congestion and consolidation of lungs*.—Signs of congestion and consolidation were occasionally observed in some cases.

(c) *Splenomegaly*.—Many earlier observers have referred to the occurrence of splenomegaly associated with eosinophilia. In the series of 16 cases it was found that 8 cases showed splenic enlargement. In one case the enlargement was considerable, in 2 cases it was very slight while in the remaining 2 cases it was moderate. The enlarged spleen is found to be rather soft on palpation with slight tenderness. With the natural exacerbations occurring in the course of the disease, splenic tenderness becomes marked. Retrogression of splenic enlargement was seen by treatment but the process was very slow.

(d) *Lymphadenopathy*.—Cervical and axillary lymphadenopathy was recorded by Patel (1945). Two out of 16 cases in my series showed well-marked enlargement of cervical, axillary and inguinal glands. The glands were found to be hard and discrete. Tenderness was not observed. The glandular enlargement disappeared very slowly with treatment.

(e) *Mesenteric adenitis*.—One case presented enlargement of mesenteric glands along with generalized adenopathy. The mesenteric glands were markedly palpable and tender. These glands became much reduced in size by arsenical treatment.

(f) *Pleurisy*.—Three of the cases studied showed evidence of pleurisy during the course of the disease. This however cleared up even before the full course of treatment was given.

V. Laboratory Investigations

(a) *Leucocyte count*.—The total count in the series varied from 13,500 to 48,000 and the eosinophil percentage varied from 19 to 74. No relationship could be discerned between the total count or eosinophil percentage and the lesions discovered on physical examination or the extent, distribution and nature of pulmonary shadows seen on radiological examination. Likewise total leucocyte count or the eosinophil percentage could not be taken as an index of the severity of symptoms like pyrexia, cough or expiratory dyspnoea.

(b) *Examination of sputum*.—Sputum on examination revealed clumps of eosinophil cells, fair number of lymphocytes and epithelial cells and rarely Charcot-Leyden crystals and Curschmann's spirals. The sputum was negative for acid-fast bacilli except in those cases where tuberculous infection was superimposed. Spirochaetes were not observed. Elastic fibres were not seen in sputum except in those cases associated with tuberculous infection.

(c) *Erythrocyte sedimentation rate*.—This was invariably raised in all cases varying from 18 to 42 mm. per hour.

(d) *Tuberculin test*.—Mantoux's intradermal test with 1 in 10,000 old tuberculin was done in all cases. Eight cases gave a positive reaction while the remaining were negative.

(e) *Histamine sensitivity test*.—In view of the assertion by Frimodt-Möller and others that the syndrome is allergic in origin it was decided to test the sensitivity to histamine in all cases. The procedure consisted of intradermal injection of 0.01 c.c. of 1 in 10,000 solution of histamine acid phosphate using saline as control. The presence of local reaction was looked for within 24 hours. Only 2 frank positive reactions and 2 doubtfully positive cases were observed in the total of 16.

VI. Radiological Findings

Radiological examination of chest invariably showed some lesions of one type or other in the

lungs. These lesions may be missed by fluoroscopy. By far the majority of skiagrams showed diffuse mottling of the lungs. These lesions are bilateral and more or less symmetrical. They were particularly marked at the hilar region and bases. An average single focus is about the size of a split pea, with a central dense zone and a comparatively light ill-defined and blurred outline. The mottling is thus of a coarser nature than that of miliary tuberculosis and moreover the single focus of miliary tuberculosis does not show the distinction in density between the central and peripheral zone as described above. The shadows may have a superficial resemblance to those of early pneumoconiosis or secondary malignant deposits. Larger and coarser shadows are also not infrequently observed. In addition to mottling prominent linear striations of the finer lung marking, symmetrically distributed in both lungs, were also seen. These indicate bronchitic or broncholytic reaction. Occasionally instead of discrete mottled shadows, linear markings of increased density radiating from the hilum are seen or diffuse fan-shaped streakings of ground glass appearance are observed. Reticular infiltration was seen in 2 cases while evidence of pleurisy was discernible in a small proportion of cases.

VII. Diagnosis

This is often difficult on clinical grounds alone. Blood examination and radiology would usually be necessary for the diagnosis. However, cough which eventually becomes paroxysmal with asthma-like attacks and progressive loss of weight with or without pyrexia would lead one to suspect this syndrome. Splenomegaly and lymphadenopathy, if present, would be of additional diagnostic significance. The occurrence of hæmoptysis early in the course of cough unassociated with fever should be viewed with suspicion as being produced by this syndrome.

In the differential diagnosis other causes of asthmatic bronchitis, eosinophilia and pulmonary shadows are to be considered.

In the typical bronchial asthma, high leucocytosis is rarely encountered and the eosinophil percentage is rarely very high. Moreover, the paroxysms of dyspnoea are very severe with much anxiety, restlessness and sense of suffocation. The allergic bronchitis resulting from inhalation of dust, fungi or other allergens can also produce eosinophilia of 10 to 20 per cent and the differential diagnosis may then be difficult. The history of allergy in family, rhinitis and other allergic manifestations in the patient should be taken into consideration.

Loeffler's syndrome is distinguished by being a mild transient eosinophilia, without splenomegaly, with fleeting pulmonary shadows shown by radiology and having a tendency for spontaneous speedy recovery.

Eosinophilia also occurs in allergic states induced by infection with round worms, filaria,

echinococcus, and in trichiniasis, brucella infections, etc. In skin diseases, such as eczematoid neurodermatitis, pemphigus, psoriasis and dermatitis herpetiformis, the eosinophils may be increased but not so high as to give difficulty in differential diagnosis.

The pulmonary shadows in the skiagrams have to be distinguished from those of miliary tuberculosis, pulmonary congestion in cardiac diseases and miliary and sub-miliary densities occurring in mitral stenosis. The nature of the shadows with its central zone of density with comparatively light peripheral zone with blurred outline should be of help in distinction.

VIII. Treatment

(a) Sulphanilamide group of drugs had been tried in adequate doses in some cases with no apparent benefit. A temporary improvement in fever was noted in some cases but the fever again appeared and ran as typical to the course of the disease. Neither the symptoms nor the eosinophilia were affected by sulphanilamide or its derivatives.

(b) Auto-hæmotherapy suggested by some observers was also tried in 3 cases with no appreciable effect.

(c) Organic aromatic arsenicals gave uniformly good results in all cases studied. Acetylarsan, neoarsenobillon and neohalarsine were used in the cases treated. N.A.B. was used in doses of 0.2 gm. to 0.4 gm. given weekly for six weeks. Weingarten suggested the drug to be administered dissolved in 10 c.c. of 10 per cent calcium gluconate solution with 200 mg. of vitamin C. This procedure was not adopted in these cases, nor was it found to be particularly necessary. After the first or more often after the second injection, a flare-up of subjective symptoms is noted with an actual increase of total leucocytes and eosinophils. In most cases the fever may rise up to 103°F. persisting for three or four days. Symptoms of vasomotor instability are occasionally encountered. These symptoms gradually abate, and with the next injection no reaction is seen. The patient experiences subjective improvement, and the improvement may be so much that some of the out-patients may not return for further treatment. The necessity of completing the treatment must however be impressed on the patient. After six injections the total white cell count falls down to a figure between 10,000 and 15,000 with eosinophil percentage from 10 to 15. Complete restoration of the white cell count and eosinophil percentage to normal has not been seen in any case. Persistence of eosinophil count a little about normal does not however give rise to any subjective symptoms. The increase of weight becomes steady, clinical and radiological signs clear up and splenomegaly as well as lymphadenopathy gradually disappear. In one case, neohalarsine injections 0.04 gm. to 0.06 gm. were given weekly for six weeks. The response was as good as in the case of

N.A.B. Intramuscular injections of acetylarsan were given in 6 cases. Flare-up of symptoms was less marked and a greater tolerance was observed without any reduction in efficiency. Acetylarsan is particularly useful in women and children.

(d) *Penicillin*.—Three cases were given penicillin 30,000 units every four hours until 12-lac units were administered. In 2 cases no effect was seen at all. In one case the reduction of fever was remarkable. Total white cell count came down to 13,000 from 21,000 and eosinophil count was reduced to 13 per cent from 19 per cent. Although this case later on required arsenical treatment for complete amelioration of symptoms and clearing of pulmonary shadows as seen in the skiagram, penicillin produced some but definite improvement. It is not proposed to draw a conclusion from this isolated case, but it signifies that further trials with penicillin in increased dosage are definitely indicated. If penicillin is demonstrated to be useful in the treatment, it may also indirectly throw light on the ætiology of the disease.

IX. Discussion—Pathogenesis

There is no doubt that eosinophil cell plays a definite rôle in the immunity mechanism of the body although much work remains to be done to elucidate all facts in relation to its rôle. The eosinophil count is high in allergic states produced by ascariasis, filariasis, trichiniasis, brucella infections, etc. In addition, eosinophilia is observed in periarteritis nodosa, polymyositis, benzene and nirvanol poisoning, and after injections of liver extract, acetylcholine, insulin, etc. But high eosinophilia with pulmonary shadows were observed first by Loeffler and described as Loeffler's syndrome. Frimodt-Møller and Barton have however demonstrated that 'Tropical Eosinophila' is different from Loeffler's syndrome in many respects. This has been already referred to under 'diagnosis'. The tendency at present is to regard 'Tropical Eosinophila' as a distinct clinical entity although its ætiology is still obscure. Frimodt-Møller believed that the condition is allergic in nature. The condition being benign, there are no reports of pathological studies of the condition except that of Meyenburg (1942) who has recorded autopsy findings in 4 patients, 3 of whom died soon after sustaining injuries and one due to tetanus. He found pneumonic foci in the lungs of varying extent and distribution. Microscopically all lesions showed a high-grade eosinophilia in the exudate. Plasma cells, lymphocytes, giant cells and alveolar epithelial cells were also found. Two cases showed eosinophilic bronchitis and bronchiolitis. Eosinophilic infiltration was also found in the liver and epididymis in 2 cases.

Weingarten did not accept the allergic interpretation of the syndrome. In the series of cases studied by the writer sensitivity to

histamine was tested and it was found that only 2 gave positive reactions. According to the histamine theory of allergic reactions it is alleged that the factor responsible for symptoms is histamine. As only 2 out of 16 cases reacted to histamine, it is evident that allergy is not the determining factor in the majority of the cases. The long and characteristic course of the disease, the definite pulmonary shadows seen in x-rays, splenic enlargement, lymphadenopathy, constant and high leucocytosis and the response of treatment with retrogression of the pathological lesions are points against allergy being the ætiological factor. The present trend of opinion is to regard the syndrome essentially due to an infection, although the nature of the infection is obscure. It is observed that eosinophilia may be found in association with some virus diseases, and hence in the production 'eosinophilic syndrome', virus ætiology is a possibility. Viswanathan and Natarajan (1945) have tested sera from 61 cases of tropical eosinophilia for cold agglutinins. Of these 53 gave positive cold agglutination, the titre varying from 1 in 16 to 1 in 2,048 and 27 of them giving high titre values about 1 in 256. Such high titre values were observed in primary atypical pneumonia which at present is regarded to have a virus ætiology. Menon (1946) brought forward some experimental evidence based on guinea-pig inoculation with blood from eosinophilic patients in support of an infective origin of the syndrome. Further work on these lines is however indicated.

Much interest has been aroused by the report of Carter, Wedd and d'Abrrera (1944) regarding the occurrence of mites in human sputum and the observation that some of these mite-infested cases showed eosinophilia. Various species of mites have been detected in Ceylon in the sputum of persons receiving treatment for respiratory diseases. The identified species included tyroglyphus, carpoglyphus, glycephagus and tarsonemus. In 3 of the mite-infested patients, an eosinophilia of 38 to 66 per cent was observed. In all of these the chest condition improved and the eosinophilia was much reduced by arsenical treatment. As mites are not susceptible to arsenic, they probably act as vectors of the infective agent. Continuation of investigation in this line would be desirable.

It has been mentioned under 'treatment' that one of the cases showed some response to penicillin therapy. Further trials with penicillin in increased doses would be required to pronounce a definite opinion regarding the use of penicillin. If, however, the causal agent of this syndrome is proved to be susceptible to penicillin and in view of the specific action of arsenic, it would not be improbable that a spirochæte may be the responsible agent. Cultural examination of the sputum of the patients for spirochætes would be another necessary line in which further investigation should proceed.

X. Summary and Conclusions

(a) A detailed analytical study of 16 cases of 'tropical eosinophilia' is presented. The available literature on the subject is reviewed and its pathogenesis is discussed.

(b) The association of cutaneous manifestations, gastro-intestinal symptoms and mesenteric adenitis with this syndrome (which has not been stressed by earlier observers) is recorded.

(c) Splenic enlargement, lymphadenopathy, cutaneous manifestations and gastro-intestinal symptoms are more commonly observed in children.

(d) Sensitivity to histamine has been seen only in 12.5 per cent of cases.

(e) The uniform response of the syndrome to organic arsenicals has been confirmed. One case showed some response to penicillin therapy. The flare-up of the symptoms during the early part of treatment is noted.

(f) The ætiology of syndrome is still obscure, but the original allergic theory of Frimodt-Møller does not seem to be tenable in the light of recent observation. The justification of the present trend of opinion towards an infective origin is stressed. The need for pursuing investigations by inoculation experiments to establish a virus origin and cultural examination of sputum for detecting any spirochæte and biopsy studies of enlarged lymph nodes is urged.

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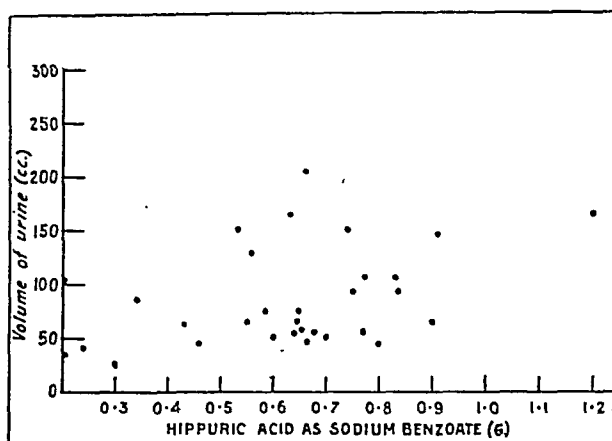
OBSERVATIONS ON THE INTERPRETATION OF THE HIPPURIC ACID SYNTHESIS TEST OF LIVER FUNCTION

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THE synthesis of hippuric acid by a process of detoxification of benzoic acid by its conjugation with glycine is now widely used as test of liver function. The synthesized hippuric acid is eliminated as such in the urine (except for

RELATION OF HIPPURIC ACID EXCRETED
AND
VOLUME OF URINE (TABLES I, II, III)



a small fraction which is also excreted in the urine but which is conjugated with glucuronic acid and eliminated as glucuronic acid monobenzoate). Preformed glycine is not available in the body and the liver has a maximum hourly synthesis of endogenous glycine. In the absence of exogenous glycine the amount of hippuric acid synthesized will depend upon the ability of the liver to produce glycine because the sodium benzoate ingested in the course of the test is in excess of the amount which can combine with the maximum amount of glycine produced. Any liver damage will adversely affect the synthesis of glycine (since liver is the site of synthesis of glycine) and the output of hippuric acid will be diminished accordingly, thus serving as an index of hepatic damage.

The test is not without limitations and too often a low result is attributed to liver dysfunction without taking into account other factors involved as will be explained later. Till now operation or necropsy findings having provided the only certain diagnostic proof, correct evaluation of the test has not been possible. I have used the needle biopsy of liver (Tripoli and Fader, 1941; Hoffbauer, Evans and Watson, 1945; Wahi, 1946) to study liver histology from freshly fixed material in a number of cases where the hippuric acid synthesis test was also performed. The difficulties in the interpretation at once become apparent. A critical review of the test is given.

Methods

Two methods are available—oral and intravenous tests. The oral hippuric acid excretion test, though very simple to perform, has certain disadvantages. Nausea and vomiting are produced, and sodium benzoate might be lost by vomiting. Besides it takes five hours to perform the oral test. The intravenous technique of Quick *et al.* (1938) has been used by the author. The patient is allowed a light breakfast. An 8.85 per cent solution of sodium benzoate is made up; 20 c.c. of this containing 1.77 g. of sodium benzoate (equivalent to 1.5 g. of benzoic acid) is injected intravenously. The injection is given slowly in 5 minutes. Immediately after injection and again an hour later the bladder is emptied. The whole one-hour specimen is used for determination. The patient is given one pint of water to drink to ensure an adequate amount of urine. This is all the more necessary in summer months.

Analysis.—The volume of urine is measured. If it is large, the urine is acidified with acetic acid and boiled until the volume is less than 200 c.c. The specimen is then acidified with concentrated sulphuric acid until it is acid to congo red. The urine is stirred well until the precipitation of hippuric acid is complete and it is allowed to stand for an hour at room temperature. The precipitate is filtered in a small Buchner funnel with a weighed filter paper and is washed with the filtrate.

The hippuric acid on the filter paper is weighed or titrated with N/5 sodium hydroxide, using phenolphthalein as an indicator. The quantity of hippuric acid that remains in solution is calculated from the volume of urine and known solubility of hippuric acid in urine (0.33 g. per 100 c.c. of urine). The result may be converted to benzoic acid by multiplying by 0.68. This is the easiest method of carrying out this test. Certain modifications have been made to make the test more accurate.

Weichselbaum and Probst (1939) pointed out that the solubility of hippuric acid in urine being not constant at room temperature, the figure of 0.33 g. per 100 c.c. is erroneous. They have tried to minimize these errors by saturation of urine with sodium chloride (30 g. of sodium chloride in 100 c.c. of urine). This is dissolved by heating and the urine is filtered. The filtrate is made acid to congo red with 50 per cent sulphuric acid and an excess of 1 c.c. is added. The flask is left overnight in the ice-box. Next day hippuric acid crystals are filtered off with suction and are washed with 20 c.c. of 30 per cent sodium chloride solution. The crystals dissolve rapidly in distilled water on washing. The solution is titrated against N/5 sodium hydroxide, using phenolphthalein as an indicator.

Allowing for 0.1 g. of hippuric acid remaining in every 100 c.c. of urine saturated with sodium chloride and for the hippuric acid dissolved by

the 20 c.c. of saline wash, the hippuric acid excreted in grammes may be calculated as follows :—

$$(\text{c.c. of } 0.5 \text{ N NaOH} \times 0.072) + \frac{0.1 \times (\text{c.c. of urine} + 20)}{100}$$

Quick (1939) has also modified his technique. He adds 5 g. of ammonium sulphate for 10 c.c. of urine before adding hydrochloric acid. The hippuric acid dissolved in urine is only 0.1 g. per 100 c.c.

The most important practical difficulty is that in some cases hippuric acid is not precipitated from urine even after saturation with salt and acidification. When a low excretion is expected the sample of urine should be evaporated down to 50 c.c. Less hippuric acid will then be held in solution and more become available for precipitation (Sherlock, 1946). Dark urine should be decolorized by boiling for a few minutes with Norit or charcoal. The specimen is then filtered (Weichselbaum and Probst, *loc. cit.*). Any protein is removed by boiling the slightly acidified urine and filtering. Finally a weighed amount of hippuric acid is estimated and by subtraction the amount in the original sample is determined (Sherlock, *loc. cit.*).

In some cases even with these precautions complete precipitation does not take place, either because the hippuric acid is too scanty or because a protective colloid is present.

Results in Normal Subjects

Intravenous hippuric acid test was carried out on 10 healthy persons (table I). The hippuric acid is expressed in terms of sodium benzoate.

The mean of the normal figure is 0.749 g. and the range is 0.64 g. to 1.2 g. These figures represent a lower range than those quoted by Quick (1939) who gives the range of 0.7 g. to 0.95 g. and Sherlock (*loc. cit.*) who gives a range of 0.75 g. to 1.21 g. These low figures in

TABLE I

Caste, sex and age	Hippuric acid (g.)	Volume of urine (c.c.)
H., M., 28	0.64	52
H., M., 26	0.84	91
H., M., 25	0.77	57
H., M., 26	0.68	56
H., M., 27	0.65	79
H., M., 34	0.65	56
H., M., 26	1.2	168
H., M., 26	0.77	106
H., F., 20	0.64	66
M., M., 26	0.7	50

Indians are probably due to a lesser excretion of urine especially in summer months.

Low results for hippuric acid synthesis have been reported in diseases which do not affect the liver. The various authors mentioned by Sherlock (*loc. cit.*) have reported as follows: Fouts *et al.* (1937), Henderson and Splatt (1942) anaemia; Moser *et al.* (1942) pregnancy and diabetes mellitus; Paulson and Wyler (1942) gastro-enteric malignant disease not involving liver; de Lor and Reinhart (1940) general infections and debilitating diseases; Higgins *et al.* (1944) myelomatosis, carcinoma and thyrotoxicosis; Campbell (1942) after surgical operations on patients without biliary disease; and Sherlock (*loc. cit.*) in anaemias of various types, diabetes, pneumonia and malignant diseases not involving liver.

My findings have confirmed the above reports that low figures of hippuric acid are obtained in some of the non-hepatic diseases, e.g. essential hypertension and pernicious anaemia. In each of these cases renal function was normal and an adequate amount of urine was assured by giving the patient a pint of water to drink before the test.

TABLE II
Hippuric Acid Synthesis in Non-Hepatic Diseases

Case	Age, caste and sex	Weight	Clinical diagnosis	Blood urea (mg./100 c.c.)	Urine urea (%)	Urea clearance (%)	Urine vol. (c.c.)	Hippuric acid (g.)
1. P. D.	45, H., M.	6 st. 9 lb.	Emphysema lung	30				
2. C. S.	42, H., M.	7 st. 6 lb.	Chronic bronchitis with gastritis and pernicious anaemia.	28	2.6 2.0	100 102	204 47	0.66 0.66
3. M. N.	46, H., M.	10 st. 7 lb.	Essential hypertension	36	2.8	100	46	0.46
4. M. K.	36, M., M.	6 st. 10 lb.	Atrophic gastritis and pernicious anaemia.	39	1.8	157	130	0.56
5. I. Z.	17, M., M.	6 st. 7 lb.	Pulmonary tuberculosis	32	1.1	79	164	0.63
6. P. S.	35, H., M.	8 st. 3 lb.	Splenomegaly. Chronic malaria?	40	1.5	75	147	0.91
7. I. M.	22, H., M.	7 st. 6 lb.	Pyrexia	43	2.9	101	43	0.8
8. S. S.	50, H., M.	7 st. 12 lb.	Non-syphilitic hemiplegia.	33	3.2	101	105	0.83
9. P. S.	40, H., M.	6 st. 2 lb.	Pulmonary tuberculosis	40	2.6	80	66	0.9
10. M. S.	32, M., M.	5 st. 6 lb.	Sciatica	36	2.5	88	96	0.75

Effect of Impaired Renal Function on Hippuric Acid Test

Both kidneys and the liver take part in the metabolism of hippuric acid. This is the main cause of confusion and difficulties in the interpretation of the test. The synthesis of hippuric acid was first demonstrated by Bunge and Schmeidenberg (Hawk and Bergeim, 1942) by perfusing the kidneys of the dogs with benzoic acid and glycine. They concluded that the kidney was the site of synthesis. In man, kidney hypofunction is associated with impaired excretion of hippuric acid (Violle, 1920). Bryan (1925) used the hippuric acid test to determine renal function. Kohlstaedt and Helmer (1936), and Henderson and Splatt (*loc. cit.*) mentioned a number of cases where low kidney function (impaired urea clearance) was associated with low hippuric acid excretion. Sherlock (*loc. cit.*) mentioned 9 cases where low hippuric acid excretion was due to impaired renal function rather than liver damage. Synthesis of hippuric acid in the kidney is questionable; but for its excretion adequate renal function is definitely required. Examination for kidney function should always be done in conjunction with the hippuric acid test. Quick (1940) suggested a coincident determination of the non-protein nitrogen of the blood. Kohlstaedt and Helmer (*loc. cit.*) and Moser *et al.* (*loc. cit.*) recommended urea clearance test. Riddell and Anderson (1944) arguing that simultaneous performance of urea clearance test makes the whole thing complicated advocate that

exclusion of albuminuria before doing the hippuric acid test should suffice. Sherlock (*loc. cit.*) did in her 9 cases the one-hour urea clearance test. In the series of cases shown in table III, the two-hour consecutive urea clearance test has been performed in conjunction with the hippuric acid test.

Cases 1 and 3 to 10 had raised blood urea and low urea clearance. These cases had low hippuric acid excretion due to kidney hypofunction rather than liver damage and confirm the findings of Snapper and Grunbaum (1924) and Sherlock (*loc. cit.*) who pointed out that azotemia is associated with impaired hippuric acid excretion and that this test should not be used as an index of hepatic function in such conditions. Besides kidney diseases, the low urea clearance (apparent) may also be due to incomplete emptying of the bladder at the end of the test. Strictly speaking the patient should be catheterized, but as most patients do not like this, it has been omitted.

In cases where low urea clearance is associated with normal blood urea, the test may be repeated the next day. Urine should be collected by catheterization. Case 2 serves as a good example. The patient had normal urine and blood urea but a low urea clearance and hippuric acid excretion. The test was repeated next day. On the second day the urea clearance was normal and hippuric acid was also normal. Sherlock (*loc. cit.*) mentions that a transitory impairment of concentrating power may occasionally develop in otherwise normal kidneys,

TABLE III

Intravenous Hippuric Acid Test in Patients without any Liver Diseases but with Apparent Renal Inefficiency

Case	Age, caste and sex	Weight	Clinical diagnosis	Blood urea (mg./100 c.c.)	Urine urea (%)	* Renal efficiency (%)	Urine vol. (c.c.)	Hippuric acid (g.)
1. B. D.	20, H., M.	7 st. 2 lb.	Syphilitic arthritis ?	53	1.8	70	150	0.53
2. H. N.	21, H., M.	6 st. 9 lb.	Gout ?					
			Giardiasis and anaemia	30	2.3	57	66	0.57
3. C. B.	45, H., M.	6 st. 7 lb.				80	150	0.74
			Ankylostomiasis with microcytic hypochromic anaemia.	50	1.4	40	86	0.34
4. S. L.	55, H., M.	8 st. 9 lb.	Endemic ascites ?	72	1.5	45	40	0.24
			Cirrhosis ? (Liver normal as revealed by biopsy.)					
5. N. S.	35, H., M.	9 st. 2 lb.	Chronic bronchitis with secondary heart failure.	61	1.2	56	61	0.43
6. M. N.	50, H., F.	4 st. 7 lb.	Subacute nephritis	107	0.7	12	101	0.2
7. N. S.	28, H., M.	8 st.	Chronic nephritis	65.8	1.7	28	32	0.2
8. B. S.	35, H., M.	9 st. 10 lb.	Endemic ascites ?	59	2.8	55	50	0.6
			Cirrhosis liver ? (Biopsy showed liver histology normal.)					
9. N. P.	35, H., M.	6 st. 9 lb.	Double mitral	57	2.2	53	27	0.3
10. F.	18, M., M.	5 st.	Double mitral with aortic regurgitation and heart failure.	53	2.2	56	75	0.59

* Renal efficiency in terms of percentage of normal clearance.

giving rise to an abnormal urea clearance and a low hippuric acid excretion.

Coincident urea clearance test should form a part of the hippuric acid test. It would determine the renal function as well as provide an indication to possible faults in collection of urine. Cases 4 and 8 were diagnosed as endemic ascites (cirrhosis liver?). The hippuric acid excretion was low and would have confirmed the diagnosis of cirrhosis of the liver but for the coincident renal function test which showed kidney hypofunction. The low hippuric acid excretion was due to kidney disease rather than to liver damage. This was confirmed by biopsy which showed the histology of the liver to be normal.

Cases 5, 9 and 10 present another interesting problem. They had congestive heart failure and as such both the liver and kidney were congested and their function lowered. The low excretion of hippuric acid may be due to combination of both factors. The significance of the hippuric acid test in heart failure cases will be dealt with in detail later.

Some of the cases detailed in table IV present a very interesting study. Cases 1, 8, 20 and 21 were diagnosed as endemic ascites. The hippuric acid test gave low figures indicating liver damage probably cirrhosis. Biopsy confirmed the diagnosis of portal cirrhosis.

Case 2 is the reverse of the above. The patient had ascites and a diagnosis of endemic ascites—cirrhosis liver (?) was made. The hippuric acid test gave normal figures, indicating that the liver was not damaged and that the patient was a genuine case of endemic ascites. Biopsy showed the liver histology to be normal.

Hippuric Acid Excretion and Volume of Urine

Conflicting opinions exist regarding the relationship of hippuric acid excretion to the volume of urine. Snapper and Grunbaum (*loc. cit.*) and Machella *et al.* (1942) quoted by Sherlock (*loc. cit.*) indicated a direct relationship between excretion of hippuric acid and volume of urine excreted by the kidneys. Boyce and McFetridge (1938) and Probststein and Londe (1942) contradicted this saying that in normal subjects no relation existed between urine volume and hippuric acid excretion if the concentrating power of the kidneys is maintained.

Sherlock (*loc. cit.*) found no relationship between the weight of hippuric acid synthesized and the volume of urine passed. She repeated the test in 14 subjects after a water diuresis. The difference between hippuric acid means was not significant. In the 14 instances for a mean urinary volume of 86 c.c., the mean hippuric acid excretion was 0.88 g., and when urinary

TABLE IV

Intravenous Hippuric Acid Test in Patients of Liver Diseases as Confirmed by Liver Biopsy

Case	Age, caste and sex	Clinical diagnosis	Liver biopsy findings	Hippuric acid excretion (g.)
1. B.	45, H., M.	Endemic ascites	Subacute hepatitis	0.54
2. C.	60, H., M.	Cancer liver	Extra hepatic biliary obstruction.	0.25
3. O. P.	25, H., M.	Cirrhosis liver with jaundice	Portal cirrhosis	0.28
4. M.	20, H., F.	Chronic malaria and ascites (tuberculosis).	Portal cirrhosis	0.28
5. D. D.	50, H., M.	Cancer liver	Adenocarcinoma liver	0.4
6. T. S.	42, H., M.	Cancer liver	Adenocarcinoma liver	0.43
7. R. S.	20, H., F.	Amoebic hepatitis	Biliary cirrhosis	0.46
8. R. L.	20, H., M.	Endemic ascites	Portal cirrhosis	0.35
9. M.	35, M., F.	Cancer liver	Adenocarcinoma liver	0.17
10. D.	15, H., M.	Chronic malaria with enlarged liver (malarial cirrhosis?).	Reticuloendotheliosis of liver	0.9
11. S. S.	40, H., M.	Endemic ascites. Cirrhosis liver?	Normal liver histology	0.84
12. S.	38, H., F.	Amoebic hepatitis	Portal cirrhosis	0.33
13. L.	45, H., M.	Ascites due to cirrhosis of liver.	Tuberculosis of liver and tuberculous peritonitis.	0.5
14. N. K.	22, H., M.	Chronic malaria	Reticuloendotheliosis	0.65
15. D. J.	56, H., M.	Hepatomegaly	Metastatic cancer of liver	0.49
16. S. D.	44, H., F.	Cancer liver	Adenocarcinoma liver	0.255
17. L.	40, H., F.	Amoebic hepatitis	Subacute hepatitis	0.598
18. P. L.	45, H., F.	Cancer liver? Cardiac cirrhosis?	Portal cirrhosis	0.6
19. M. P.	20, H., M.	Hepatomegaly	Subacute hepatitis	0.25
20. C. L.	30, H., M.	Endemic ascites	Atrophic cirrhosis of liver	0.27
21. P. L.	50, H., M.	Endemic ascites	Portal cirrhosis of liver	0.22
22. S. N. D.	27, H., M.	Amoebic hepatitis	Amoebic abscess. (Puncture done.)	0.19
23. J. N.	22, H., M.	Endemic ascites	Liver biopsy failed	0.22
24. R. S.	32, H., M.	Chronic malaria with cirrhosis of liver.	Subacute hepatitis	0.46
25. R. D.	30, H., F.	Hepatomegaly with splenomegaly. Chronic malaria?	Portal cirrhosis	0.57

volume became 439 c.c., the mean excretion became 0.92 g.

Body Weight and Hippuric Acid Excretion

Quick (1931) stated that, if glycine be given with sodium benzoate, the excretion of hippuric acid reaches a maximum varying with a size of the individual.

Hepler and Gurley (1942) stated that the upper limit of the test depended upon the body weight. Machella *et al.* (*loc. cit.*) found no correlation between the two. Scurry and Field (1943) quoted by Sherlock (*loc. cit.*) evolved formulæ relating body weight to hippuric acid excretion as they found that sufficient relationship existed between the two. Sherlock (*loc. cit.*) studied 30 subjects and found very slight correlation. My results in 20 cases are in conformity with Sherlock's findings (tables II and III).

Hippuric Acid Excretion in Congestive Heart Failure Cases

Right-sided heart failure leading to venous congestion and anoxæmia of the liver will lead to lowered hepatic function and lowered hippuric acid excretion and should bear direct relationship to the severity of heart failure. If this is so, it opens a new field of importance of the hippuric acid synthesis test as a means of judging the prognosis in heart failure cases.

The argument against this could be that in such cases there would also be venous congestion of the kidneys resulting in oliguria and lowered hippuric acid excretion. It is questionable if the venous congestion at least in mild degrees leads to any impairment of renal function as is shown by ability to excrete urine of high concentration. Fishberg (1940) lays great importance on the loss of concentration as an indication of lowered renal function. In very advanced cases when the engorgement of kidneys is severe and oliguria is extreme sub-normal figures are not unusual.

Bearing in mind that the causation of oliguria which leads to hippuric acid retention is the same (venous congestion due to right heart failure) as the cause of lowered liver function, this test can still be used as a measure of the severity of heart failure and repeated results would be of prognostic value. The following case would support the above contention.

Patient F., a Mohammedan male, aged 18 years, was admitted and diagnosed as congestive heart failure (double mitral and aortic regurgitation). On 18th May, 1946, his hippuric acid excretion was 0.590 g. His condition became worse, œdema and oliguria increased, and on 25th May, the hippuric acid was 0.39 g. Full digitalization improved his condition considerably, and on 29th May, the hippuric acid excretion was 0.57 g. The case is still under

treatment. These figures are interesting as indicating that hippuric acid excretion varies with the degree of heart failure.

In hypertensive heart failure cases the arteriosclerotic changes in kidneys would lead to impairment of renal function and nitrogen retention. In such cases the hippuric acid test would give inconclusive results.

Discussion

The liver is generally believed to be the site of the synthesis of hippuric acid and on this assumption the hippuric acid output has been used as a liver function test. Kidney damage is to be excluded as normal excretion of hippuric acid is essential for correctly assessing the result. Cases are met with where liver and kidney functions have been demonstrated as normal and the test gave low figures. This suggests that besides liver and kidney other factors may be involved in the synthesis and excretion of hippuric acid and that this is not so infallible a test of liver function as was once supposed. Sherlock (*loc. cit.*) also came to the same conclusion.

I have performed the intravenous tests and prefer it to the oral test. It is simple and safe and takes only an hour to do. No toxic symptoms like nausea and vomiting are produced. The difficulties in the interpretation have been pointed out and should be kept in mind by the physicians and surgeons.

The cardiologist may find this test of great value in gauging the prognosis in congestive heart failure cases.

Summary

The intravenous hippuric acid test has been carried out in a number of cases with and without liver involvement and the results have been correlated with the histological appearances of needle biopsy tissue from the liver.

Tests of kidney function are a necessary adjunct to this test. The urea clearance test is preferred for this purpose.

The relation between the excretion of hippuric acid, the volume of urine and the weight of patient has been investigated.

Certain non-hepatic conditions have been found to give low results.

The value of this test as a prognostic test on cases of congestive heart failure has been discussed.

I am grateful to Professor G. N. Vyas, Dr. K. N. Gaur, Reader in Medicine, and Drs. K. S. Mathur and B. K. Dube, for giving me facilities in the ward to carry on the investigations, and to Drs. Kashi Nath and V. N. Tiwari, for the constant help in biochemistry.

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DISSECTING ANEURYSM OF THE AORTA: A CASE REPORT AND A REVIEW OF 133 CASES

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S., HINDU male, aged 45 years, was admitted to the J. J. Hospital on 27th April, 1946, at 11.30 p.m. and died on 30th April, 1946, at 11.20 p.m.

Clinical abstract.—Patient complained of (1) thumping in the chest and (2) vomiting since previous evening. There was no pain in the chest, only discomfort. There was previous history of palpitation but not of similar thumping. General examination: Poorly built and nourished. Conjunctiva pale, nails pale, tongue clear, deviates to the right, lymph glands not palpable, visible pulsation at the angle of jaw,

pulse 60, blood pressure 125/80; bones and joints normal; cardiovascular system—pulse very weak, irregular, ? extra-systole, apex beat felt in mid-clavicular line of 8th space, both mitral sounds muffled; blood: R.B.C. 4.2 millions, W.B.C. 10,900, W.R. negative, Kahn's test doubtful, but 'O' Rapid test of Rapaport and Eichon was negative.

Post-mortem notes.—On opening the body the heart was enlarged. Pericardium contained 4 oz. of blood-stained fluid. There were hæmorrhagic areas in epicardium surrounding the blood vessels. On dissection, the thoracic aorta down the aortic opening in the diaphragm consisted of double tubes one inside the other but attached to each other at places. The heart and aorta were carefully dissected out. Both the tubes contained blood, the outer contained some clots too. The inner tube was friable and showed many transverse tears about $\frac{1}{2}$ inch distal to the aortic opening. There was one large transverse tear about $\frac{3}{4}$ inch in length. The ascending aorta was dilated. Aortic valves and the aorta were atheromatous. The coronary arteries showed atheroma, and small arterial twigs of coronaries were all occluded near their openings in the parent trunk. There was a big linear scar at the junction of ascending aorta and the arch of heart. The gullet contained a nodule projecting inside the lumen of the size of a pice and a tumour feeling solid like a fibroma. Stomach contained food in very small quantity. In the stomach and the intestines there were no lesions. Tongue, tonsils, trachea, larynx and bronchi did not show any evidence of disease. Lungs were large, voluminous and heavy, pitting on pressure but non-crepitant. The cut surface showed large amount of serous froth in both lungs. The left ventricle was hypertrophied. There were no other lesions in the heart except those mentioned along with aorta and coronary artery above. Liver was scarred and lobose. The left lobe was unusually small. The scars did not go very deep beyond the surface. Gall-bladder showed thin watery bile. Spleen atrophied, kidneys healthy, prostate and sup-
 renals normal.

Body	45 kg.
Brain	1,420 gm.
Right lung	1,040 "
Left lung	720 "
Heart	590 "
Liver	1,390 "
Spleen	60 "
Kidneys	240 "
Worms	Nil.

Post-mortem diagnosis.—Coronary occlusion. Important lesions:—

- (1) Atheroma aorta and coronaries.
- (2) Dissecting aneurysm aorta beginning from ascending aorta about $\frac{1}{2}$ inch above aortic opening and the dissection is traceable up to aortic opening in diaphragm.

(3) Fibroma in œsophagus.

(4) Scarred liver.

Histology : Liver—scarred—not syphilitic; aorta—scarred—atheroma—no syphilis; fibroma œsophagus—myoma.

The above case is reported as dissecting aneurysms are found very rarely in the post-mortem room. Moreover, the type of lesion encountered is remarkably complete. This institution has careful records of all post-mortem examinations done from 1882, and a brief summary of cases of aneurysms is given below to show their relative incidence.

Six case reports of different types of aneurysms were read before the meetings of Teaching Pathologists of Bombay. At the 6th meeting in 1937 Gharpure analysed some of the data from this institution but as nearly a decade has since passed this analysis is including the work shown in the previous unpublished paper.

In a period of eight years 423 cases of sudden death were brought to this post-mortem examination room from outside to exclude medico-legal causes. Out of these 59 (13 per cent) turned out to be cases of aneurysmal ruptures, 57 were males and 2 females. The communal distribution was as under :—

Hindus	38
Muslims	18
Christians	3
Anglo-Indian	1
Jew	1

From 1882 to 3rd May, 1946, there were 10,163 post-mortem examinations done on hospital cases in this department. During this period the incidence of aneurysms amongst 133 cases was as under :—

	Total	Males	Females
Aortic	105	100	5
Heart	13	12	1
Other	15	13	2

Aortic aneurysms showed the following regional distribution :—

Ascending aorta	43
Aortic arch	38
Thoracic aorta	11
Abdominal aorta	13

The lesion extended through ascending, transverse and descending aorta in two cases and through the ascending and transverse part of the aorta in three cases. Only in one case it extended in the aorta from the beginning up to the bifurcation. The maximum size of the aneurysm of the aorta described is that of a foetal head.

The distribution of the aneurysms of the heart was throughout in the left ventricle. Only in five cases out of a total of 13 was the aneurysm located at its apex.

The distribution of aneurysms in other vessels was as follows :—

Cerebral arteries	7
Basilar	3
Anterior cerebral	1
Left middle cerebral	2
Anterior communicating	1
Other arteries	8
Pulmonary	1
Popliteal	1
Femoral	1
Common iliac	1
Splenic	1
Renal	1
Cœliac	1
Coronary	1
TOTAL	15

The lesions were in some cases at more than one place. The case of aneurysm of the splenic artery showed multiple beading with aneurysms on its whole length. In one case there were two aneurysms on the left ventricle. In another case there was an aneurysm in the femoral artery and the aorta. In the third case there was an aneurysm in the heart and common iliac artery.

Out of the 133 cases there were 16 cases that died in the admission hall before being examined. Rest of the 117 cases were admitted to the hospital. The maximum duration of stay in the hospital was 15 days, the minimum being four days. Clinical notes were not recorded for some of the early cases. But amongst the recorded cases aneurysm was suspected in only 7 cases. Rest of the aneurysms were missed clinically or found as an accidental discovery during the post-mortem examination, the death having taken place by diseases like tuberculosis, pneumonia, etc.

In the above series there were only 5 cases of dissecting aneurysm. In two cases there is no description of the extent of the lesion, but the aorta has shown atheroma in one and mesoarteritis in the other. In the third case the lesion has been described as hæmatoma in the wall of the aorta, not communicating with the lumen but the hæmatoma ruptured in the pericardium. This description suggests a dissecting aneurysm. In the fourth case the dissection has extended up to the bifurcation of the aorta. This specimen has been sectioned in two halves and is exhibited in the Museums of Pathology of both the medical colleges here. In this case though the lesion extended lower down up to the bifurcation, the dissection of the wall into two tubes was not so remarkably complete as described in this paper. The aorta of this case was so friable that it could not be successfully preserved for exhibition.

On analysing the incidence of other lesions the following data are available. The blood was taken for W.R. at the post-mortem examination in 18 cases. The results were positive in 15 and negative in 3 cases.

Out of the three negative cases one occurred in the renal artery and two in the heart.

In the aorta there was macroscopic evidence of syphilitic mesaortitis in 14 cases. There was evidence of atheroma in 8 cases. As opposed to this in 7 cases of cerebral artery aneurysms six had atheroma and one had syphilitic mesaortitis.

The incidence of ruptures was as follows :—

Abdomen	2
Thorax	6
Pericardium	18
Pleura	5
Bronchus	7
Trachea	5

The maximum size described for cerebral arteries is that of a marble. The age distribution was as follows, the minimum being 20 and the maximum 75 years.

Table showing distribution by age groups

Age group, years	Aortic	Heart	Other arteries
11-20 ..	1	0	0
21-30 ..	42	2	3
31-40 ..	67	5	5
41-50 ..	35	4	4
51-60 ..	13	2	2
61-70 ..	5	0	0
71-80 ..	1	0	0
81 and above ..	0	0	0

On going through the histology records from 1914 to 1946 the incidence of lesions in the aorta is as follows :—

Syphilitic mesaortitis	14
Atheroma	14
Aneurysms	6

Summary

A case of dissecting aneurysm is described. Records of 133 cases available from the post-mortem reports of J. J. Groups of Hospitals at G. M. College, Bombay, have been analysed.

My thanks are due to Professor P. V. Gharpure, Professor of Pathology, G. M. College, and to Lieut.-Colonel Jelal M. Shah, Superintendent, J. J. Group of Hospitals, Bombay, for allowing the use of records.

AMŒBIC HEPATITIS AND ASSOCIATED PERICARDITIS

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ONE of the rare complications of amœbiasis is pericarditis. According to Kern (1945) a review of literature revealed 22 proved cases of amœbic pericarditis. The case described by him was secondary to extension of amœbic abscess of the liver, and the correct diagnosis was made only at autopsy.

The case reported here was one of amœbic hepatitis and associated acute dry pericarditis. The pericarditis was secondary to extension of the hepatitis. The patient was cured with injections of emetine hydrochloride. The rarity of the incidence of amœbic pericarditis secondary

to amœbic hepatitis warrants the present publication.

Case history

K. K., 17 years, Hindu female, married, was admitted to Shri Janki Devi Bhagat Mahila Seva Sadan, Agra, for confinement. She delivered a living child who suffered from infantile diarrhoea and expired after 25 days. She started running a temperature 2 days after the confinement. An intramuscular injection of quinine bihydrochloride (10 grains) was given, but the temperature persisted. An examination of her vaginal smear showed pus cells in large number, a few extra-cellular Gram-positive diplococci, staphylococci and Gram-negative bacilli. A diagnosis of puerperal sepsis was made and she was put on sulphanilamide tablets of which she got a total dose of 40 grammes. In spite of this her temperature continued. At this stage a clinical diagnosis of typhoid fever was entertained. The following investigations were done : Blood : Total white cells 7,450 (polymorphonuclears 72 per cent, lymphocytes 22 per cent, large mononuclears 3 per cent, eosinophils 3 per cent); no parasites. Urine showed nothing of significance. Widal test (18th day of fever) was negative against typhoid and para-typhoid groups of organisms. The author was consulted on the 27th day of fever when clinical examination revealed as follows : Patient was of average health. No toxæmia, temperature 104.4°F., pulse 104 and respirations 20 per minute. The temperature chart showed that she was having intermittent fever ranging from 98.2°F. to 103.4°F. Tongue was coated. Liver was enlarged 2 inches below the costal margin and actually tender; upper border was on the 5th rib along the right mid-clavicular line. Pressure into the intercostal spaces over the liver elicited severe tenderness. Cardiovascular system : Blood pressure was 104/72; apex beat was in normal position; sounds were normal in all the areas; diffuse, loud and creaking pericardial friction rub was heard over the præcordium, being most prominent towards the right border of the heart; there was no endocardial murmur in any area. Respiratory system :—Right side (back) middle and lower zones showed diminished movement, diminished vocal fremitus, dullness, markedly diminished breath sounds, no adventitious sounds, and diminished vocal resonance. The upper zone of the right lung and the whole of the left lung were normal. Other systems were clinically normal. A diagnostic paracentesis thoracis was done on the right side but it was a dry puncture.

Progress and treatment.—Daily intramuscular injections of 1 grain of emetine hydrochloride were started. Next day the stool was examined; the report showed that it contained a large number of pus cells and a few red cells but no *Entamœba histolytica*. Gradually the liver became normal in size, the tenderness disappeared, and the right lung showed normal findings. After 3 grains of emetine the

pericardial friction rub became faint and was gradually localized at the cardiohepatic angle. It completely disappeared after 6 grains of emetine therapy. Now she was transferred to the local medical college for further investigations which were as follows: Blood: Total white cells 7,000 (polymorphonuclears 74 per cent, lymphocytes 20 per cent, large mononuclears 3 per cent, eosinophils 3 per cent); no parasites. Urine normal. X-ray of the chest normal. Movement of the right dome of the diaphragm showed limitation as examined under the screen. Stool: 3 examinations after saline showed nothing abnormal. Wassermann reaction negative. She became afebrile and was discharged cured with an increase of weight by 10 pounds.

Discussion.—The clinical picture coupled with the response to emetine established the case as one of amœbic hepatitis and associated acute dry pericarditis. The pericarditis was evidently caused by extension of inflammation of the liver. The examination of blood before emetine was started did not show leucocytosis which is of

diagnostic significance in such cases. Absence of leucocytosis was due to sulphanilamide therapy before the blood count was done. The examination of stool just after emetine was started suggested colitis, but repeated examinations failed to demonstrate *Entamoeba histolytica*. This is quite a common finding in amœbic colitis.

Summary.—A case of amœbic hepatitis and associated acute dry pericarditis has been described. The interest of the case lies in the associated pericarditis which responded to emetine.

Thanks are due to Rai Bahadur Dr. G. P. Rawat and Dr. K. M. Correa of the Shri Janki Devi Bhagat Mahila Seva Sadan, Agra, for their valuable help during the patient's stay in the Seva Sadan. Thanks are also due to Major-General H. C. Buckley, Principal, Medical College, Agra, for his permission to publish this report, and to Drs. K. S. Mathur, Lecturer in Cardiology, M. Y. Faruqi, and M. N. Kapoor, house physicians, for their helpful suggestions and co-operation.

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A Mirror of Hospital Practice

AN UNUSUAL CASE OF SNAKE BITE : INTRAVENOUS SODIUM SULPHATE TREATMENT OF THREATENED URÆMIA

By JOHN LOWE, M.D.

and

H. CHAKRAVARTI, M.B.

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THE following case seems worthy of record :—

The patient, a Bengali male, living on the outskirts of Calcutta, was standing in long grass in a field when he felt a bite upon the right big toe. He did not see what bit him; the bite bled a little; he was apparently not very alarmed.

About fifteen minutes later he noticed that the toe was swollen and painful; an hour later he felt nausea and began to vomit. Later he began to notice dark-coloured patches in his skin. He also suffered from pain in the abdomen, particularly in the right upper quadrant, and his vomiting persisted. At the site of the bite there was only slight swelling and pain and no other symptoms. That day he could take nothing by the mouth without vomiting, and his urine was small in amount and highly coloured. Later that day he became jaundiced.

On the following day the swelling of the foot subsided, but the other symptoms persisted and became more severe; the next morning, *i.e.* 48

hours after the bite, he presented himself at the hospital.

On admission the patient's general condition was fairly good. His temperature and respiration rates were normal and the heart's action was normal, there was slight bradycardia. He was moderately jaundiced, complained of abdominal pain particularly in the liver region, and vomited from time to time small amounts of fluid. In various parts of the body, mainly on the trunk and the arms, there were petechial hæmorrhages varying in diameter from one-fourth of an inch to an inch and a half. The liver was large and tender and there was slight pain in the kidney region. He said that he had passed practically no urine since being bitten.

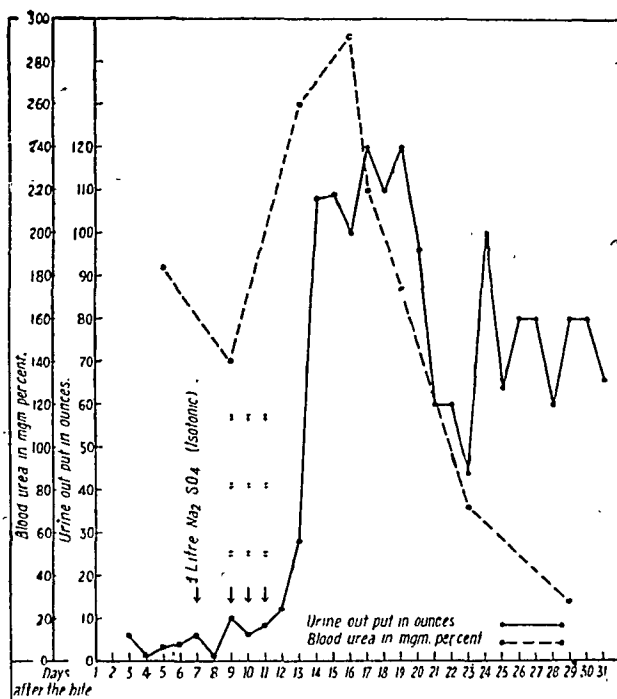
There was no appreciable swelling of the toe or foot at the site of the bite; the marks of the bite were not clearly visible (the skin of the toe was very thick and hard).

After admission to the hospital the symptoms described persisted but the jaundice rapidly disappeared and the vomiting gradually subsided. The vomit on examination showed blood. The urine on examination showed albumin and red blood cells in large amount. Blood examination showed a low red cell count ($2\frac{1}{2}$ millions) and a low platelet count 28,300. The bleeding time was $12\frac{1}{4}$ minutes, and the coagulation time 3 minutes.

For the first few days in hospital his general condition improved but a persistently low urine

(containing much blood) output was an alarming feature. The urinary output, the blood urea levels, and the treatment given are indicated in the figure (see chart).

With the persistent low urine output and the rising blood urea and the development later of general œdema, there was an obvious danger of death from renal failure. It was decided to give the intravenous sodium sulphate treatment for this condition. On each of four days, one litre of distilled water containing 1.89 grammes of anhydrous sodium sulphate (equivalent to 4.28 grammes of Glauber salt) was given intravenously. During the period of treatment the urine output rose very little, and after four intravenous injections his general condition was obviously worse, the blood urea was still rising, the œdema and ascites were marked, the patient was very gravely ill, and hopes of recovery were



almost abandoned. On the following day however his urine output began to rise and subsequent events are indicated in the chart. Recovery was uninterrupted and rapid, the blood urea and non-protein nitrogen rapidly falling to normal.

About two weeks later kidney function tests showed defective function, but in a subsequent test done few days back it was found normal.

The recovery in this case appeared to be attributable to the sodium sulphate treatment, although, as is not uncommon, the response was delayed.

The sodium sulphate treatment of anuria was fully discussed by Wade and Dick (1934) who recommended that it be given by continuous intravenous drip up to 200 c.cm. an hour for the first day, and later at 100 c.cm. an hour. This information was not available to us when treating

this patient. The doses used were much smaller and the administration lasted only about an hour each day with a day's break after the first day.

The point of diagnosis arises in this case. The history and many of the symptoms pointed very strongly to a snake bite of the viperine class, but there was the striking absence of any marked lesion at the site of the bite. This may be seen with viper bite but usually in cases in which venom is injected more or less directly into the blood stream, and in such cases rapid death is usual. The most likely explanation in the present case seems to be that the dose that was injected was quite small, possibly by a very young viper, but it entered the blood stream rapidly and was not sufficient to cause death. It failed to cause any marked local lesion but produced severe damage to liver and kidney. Vipers usually bite higher up than the toe and moreover a person bitten will usually hear the hiss of the viper which was not so in this case. These facts also suggest the possibility of a very young small viper. There is no reasonable alternative diagnosis to viper bite in this case. The circumstances would practically rule out Weil's disease.

The recovery under sodium sulphate treatment after thirteen days of almost complete anuria is remarkable.

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OCULAR COMPLICATIONS IN MALARIA: A CASE OF DENDRITIC ULCER

By G. FALCONE, M.D. (Rome)

OCULAR complications due to malaria are certainly not frequent, but it is known that under the name of larvate malaria a certain number of ocular symptoms are described which are considered as aberrant troubles. In order of frequency these are: photophobia, congestion of the bulbar and/or palpebral conjunctivæ, neuralgia of the ophthalmic branch of the trigeminal nerve that can be complicated by neuritic troubles or by herpetic eruptions. Of the same origin are reported the periodic recidivant herpes of the cornea and the chronic dendritic ulcer.

Cases of iritis, retinal hæmorrhages and various forms of diminution of vision have been described in malaria; retinal hæmorrhages occur in the cerebral pernicious form of malaria; and in the same form an amblyopia or an amaurosis may occur, accompanied by optic neuritis, peripapillary œdema and large retinal hæmorrhages.

A specific malarial toxin has not yet been demonstrated, but it is known that humoral changes occur in malaria. According to more recent views, the malarial parasite is principally acting on the reticulo-endothelial cells, and the phenomena observed in chronic malaria would lead to the recognition of the existence of a

malarial toxin. It seems that the newly discovered exo-erythrocytic stage of the malarial parasite will open a new way for the solution of the therapeutical and immunological problems of malaria (Jerace, 1939).

It is admitted, however, that allergic phenomena occur in malarial cases of urticaria (Mohanty, 1945; Stefanini, 1945) and malarial nephritis is also considered to be an allergic phenomenon due to previous sensitization of the kidneys by foreign protein and host tissue-destruction, resulting from the malarial infection (Laha, 1945).

Many authors have proved very conclusively that the tissues of the eye can be readily sensitized both locally or as a part of a general sensitization and that they are capable of allergic response. The reaction of the cornea is determined primarily by its avascularity which, in a general sense, makes it less liable to participate in acute infections and more prone to allergic reactions (Duke-Elder, 1939).

The dendritic keratitis is a not infrequent form of chronic superficial ulcer of the cornea, often appearing in connection with malaria, and is considered amongst the neurotrophic disturbances of herpes cornealis febrilis.

According to Busacca (1925), a considerable proportion of the population are herpes carriers, and any accompanying systemic infection allows the virus to establish a foothold in tissue the resistance of which has been lowered (Duke-Elder, 1939). This elective sensitization and lowered resistance of cornea in malaria may be considered of allergic nature, specially when the corneal manifestation coincides with the recrudescences of the general systemic condition.

In the dendritic ulcer the infiltration, limited to the superficial layers of the cornea, assumes the form of a zig-zag line with small lateral ramifications at the ends of which small round greyish infiltrates are noted. If the ramifications are very close from their fusion a single ulcer may occur, and this may become septic and complicated with hypopion.

The treatment is carried out on usual lines as for the corneal ulcers. Considering the accompanying condition of the corneal anaesthesia, it is wise to protect the eye with a shield that will prevent foreign bodies from damaging the cornea. As general treatment, beside the anti-neuralgic salicylates, in the cases in which malaria is active, the specific antimalarial drugs are very efficacious.

A case is reported of dendritic keratitis, associated with benign tertian malaria, and relapsing with malarial attacks. The patient has been followed by me for many months.

Case report*

M. I., male, age 39, European.

History.—At 16 typhoid. In India from 1941.

On the 23rd September, 1941, first attack of malaria (B.T.) followed by four regular ague fits. On the 5th

October, 1941, corneal herpes in left eye accompanied by ciliary pain, lacrimation, blepharospasm. Afterwards the corneal condition was complicated by a septic corneal ulcer that healed in March 1942, leaving a macula as residual scar.

During the rainy season of 1942 the patient suffered from several malarial relapses, in mild form, easily controlled by quinine. The drug was given also long after the fever ceased and no ocular trouble occurred.

On the 5th February, 1943, new relapse of malarial fever and five days later the patient came to me with a recrudescence of the dendritic keratitis in the left eye.

The examination of the left eye showed :—

Vision : Counts fingers at 1 foot. Eyelids swollen. Redness and swelling of the palpebral and bulbar conjunctivæ; intense perikeratic infection. Cornea—diffuse haziness, mostly marked in the lower portion between 4 and 8 o'clock where, with fluorescein staining, some arborescent superficial ulcerations are in evidence. The cornea is insensitive in the lower half, and the sensitivity is also impaired in the upper half. Examination of the media and fundus is not possible on account of the condition of the cornea.

After two weeks of treatment, generally with anti-malarial drugs (quinine-mepacrine-plasmoquine) and locally with atropine-dionin, the condition improved and the vision was 6/18. Both the malarial and the ocular conditions settled down after treatment.

On the 15th July, 1943, again malarial attack followed two days later by corneal reaction, both promptly cleared up with antimalarial treatment combined with instillation of atropine and dionin in the eye.

On the 12th October, 1943, a new malarial relapse was again followed by a corneal inflammation: the usual treatment was given, and the same results obtained.

After all these relapses the ocular condition in the left eye was the following :—

Vision : 6/24. Cornea : Superficial opacities cover the inferior half; some more marked ramified lines are noted. Corneal anaesthesia of the lower half, hypoaesthesia on the upper half. Nothing abnormal is noted in the media and fundus. The right eye has never been affected.

The reported case shows clearly the correlation between the malarial condition and the ocular complication.

Summary

Ocular complications are seen in malaria; the actual knowledge of the malaria parasite cycle and of the immunological phenomena in malaria are in favour of specific humoral changes: the ocular complications may be related to these changes, probably as allergic reactions.

A case of dendritic keratitis, relapsing with malarial attacks, is reported and its aetiopathology is discussed.

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PENICILLIN IN TYPHOID FEVER

By S. R. LOKRE, L.M.P.

Private Practitioner, Residency Area, Indore, C. I.

A boy of seven years, constitution healthy, was suffering from high fever which started with rigors. He was complaining of severe headache and pain in the abdomen. In the beginning he was treated by his family members with quinine and acetyl salicylic. On the fourth or fifth day of his illness when his temperature did not come down and he was in acute stage I was called in. History of malarial fever and expulsion of threadworms was elicited.

Total W.B.C.—6,700; differential count (200 cells)—polymorphonuclears 57 per cent; lymphocytes 40 per cent; large monocytes 2 per cent; eosinophils 1 per cent; basophils nil; myelocytes nil; malarial parasites—not found.

I gave two quinine injections in five grain doses for two consecutive days and saline enema for three consecutive days. Threadworms were passed but there was no reduction in the temperature and his condition did not improve. Other bacteriological examinations such as cultures of blood, urine and faeces were not practicable but because the results of therapeutic tests were negative and typhoid fever is endemic in the locality my suspicion was strongly in favour of an acute onset of typhoid fever.

On and from the 7th day of the disease he was going bad. His temperature ranged between 103°F. and 105°F.; pulse was 102 and respiration 30 p.m. Lungs were clear. He became cyanosed, a little dyspnoeic and drowsy. There was a good deal of flatulent distension, heart in fibrillation.

A more unsuitable subject for enteric fever would be difficult to find on clinical grounds. For fever a simple alkaline mixture was ordered from the beginning. Ice pad and ice cap were applied on forehead and at the nape of the neck respectively. It was clear that he was on the verge of hypertoxic condition and would prove fatal if dealt with in the orthodox fashion.

The results of experiments pertaining to penicillin sensitivity of *Bact. typhosum* suggest that a retarding effect is exercised by penicillin on the rate of growth of *Bact. typhosum* in vitro and in vivo.

I, therefore, decided to put him on penicillin. I generally add adrenaline 1 c.cm. to the bulb of penicillin solution whenever I have to use it in acute infectious diseases. Moreover, adrenaline maintains blood pressure which is absolutely necessary in all types of cases where penicillin is indicated. So during the period he was given penicillin 50,000 units with adrenaline intramuscularly every twelve hours. He received 400,000 units of penicillin in four days. When I finished the course four days later (11th day) his temperature was lowered by two degrees. He

became bright and cheerful. I then discontinued the injections for four days. The temperature was now varying from 101°F. to 102°F. One further course of penicillin was given from 15th to 18th day. Thus in all 800,000 units of penicillin were given in two courses. Even after the second course of penicillin he was keeping 100°F. temperature for two more days. After this his convalescence was normal.

In one way the case was encouraging. There could be no question that toxæmia was considerably checked with penicillin during the course of the disease and after its administration there were no complications.

PANCOAST TUMOUR

By B. L. RAINA

MAJOR, I.M.S./I.A.M.C.

FOURTEEN years ago Pancoast (1932) described a superior pulmonary sulcus tumour characterized by an apical shadow, pain in the shoulder, pain referred down the arm, atrophy of muscles of the hand, Horner's syndrome and destruction of the first two or three ribs. These cases are of apical carcinoma but are of interest in view of the absence of pulmonary signs and symptoms in the early stages of the disease.

Case Report

On 4th June, 1944, G. G., a young man, aged about 38 years, was brought to this hospital. He complained of pain in both legs, knees and ankles for the previous four months. He gave a history of primary syphilitic sore in 1936 for which he took three courses of N.A.B. injections (two courses of twenty injections at weekly intervals and third course of ten injections). Since 1937 his W.R. remained persistently negative. On examination bones of the legs showed thickening of periosteum. Lungs showed no dullness, expiration was prolonged and occasional rhonchi were heard especially after coughing. Nothing abnormal was found in any other system. B.S.R. was 100 mm. in first hour and 131 mm. in second hour.

X-ray (6.44) showed lamellated layers of sclerosed periosteum lying parallel to the shaft of all long bones, articular ends of the knees decalcified (see figures 1 and 2, plate XXXII); chest x-ray (8.44) showed signs of chronic bronchitis.

Two months later the layers of periosteum were seen fused to form thick sclerosed sheets with serrated outline. The periosteum was unevenly raised over the diaphyses of the long bones especially the distal ends of shafts.

The patient then began to complain of cough and of his bones getting wider; and x-ray taken on 21st November, 1944, showed the same changes in the bones as seen three months ago, and also revealed an opacity in the apex of the right

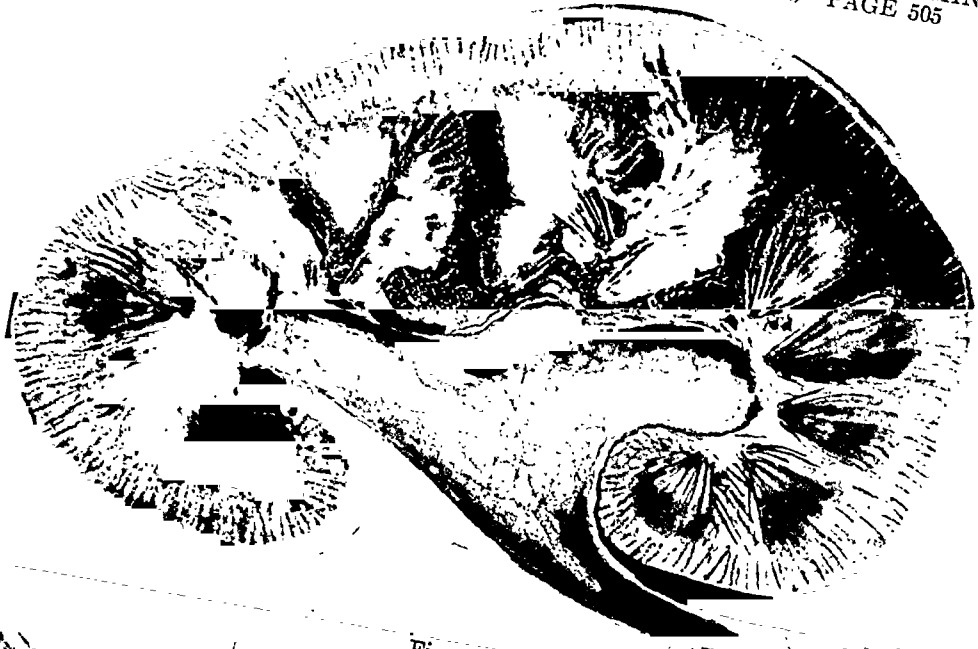
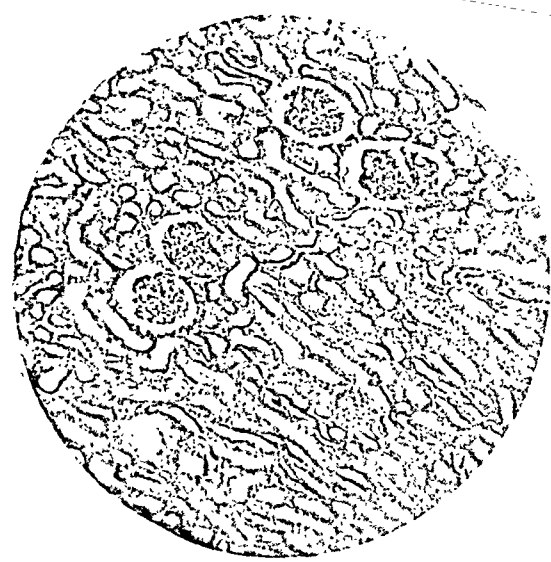
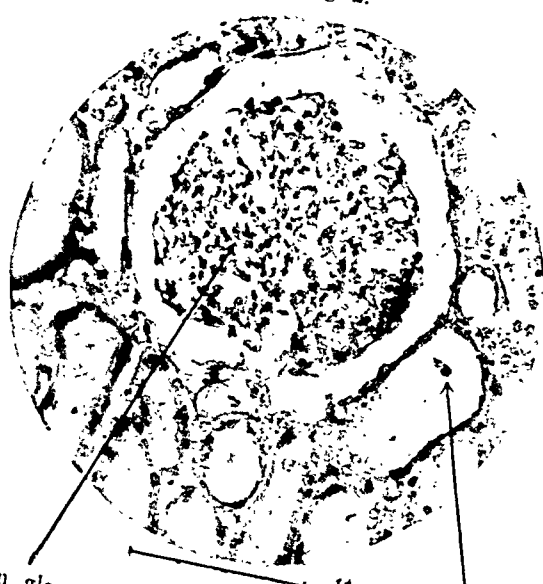


Fig. 1.



10 μ
 Fig. 2.

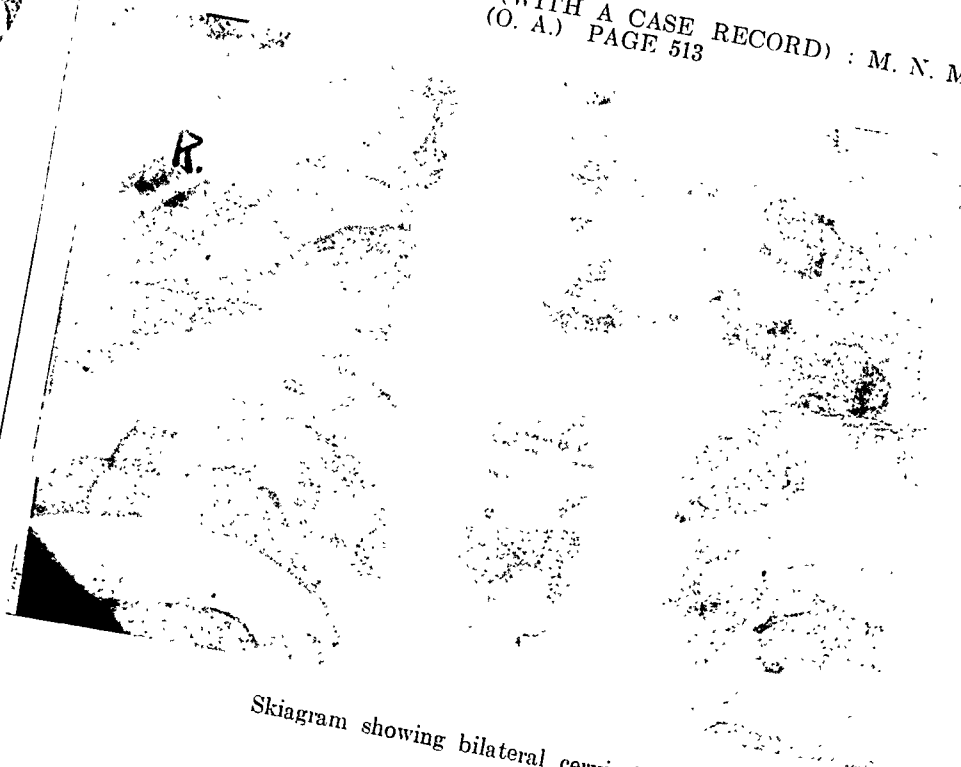


Swollen glomerulus
 with marked cellularity.

Fig. 3.

Crystalline
 deposit.

CERVICAL RIB SYNDROME (WITH A CASE RECORD) : M. N. M.
 (O. A.) PAGE 513



Skiagram showing bilateral cervical ribs.



Fig. 1.



Fig. 2.

Figures 1 and 2 showing decalcified long bones.



Fig. 3 showing opacity in the apex of the right lung.



Fig. 4.



Fig. 5.

Photomicrographs (figures 4 and 5) of the section of tumour.

lung (see figure 3, plate XXXII). In view of the history of syphilis and generalized periostitis he was given a course of anti-syphilitic treatment (injections of arsenic, bismuth and later penicillin) without any benefit.

His general condition deteriorated rapidly and he lost about 30 lb. of weight in two months. In January 1945 he complained of pain in the right shoulder shooting down the inner side of the right arm. Physical examination revealed Horner's syndrome, with slight wasting of muscles of the right supra and infraspinous regions, diminished movements above and below the right apex, dullness, bronchial breathing and crepitations in the same area. Diagnosis of pulmonary neoplasm was made and the patient was sent for deep x-ray therapy. X-ray (26th March, 1945) showed a homogeneous opacity in the right apex, marked enlargement of all terminal phalanges of fingers and toes, thickening of ends of ulna, radius, tibia, fibula and lateral half of clavicles, vertebral extremities of second and third ribs eroded, oesophagus deviated to the left and anteriorly at the sternoclavicular joints. The patient showed no improvement in his condition and died on 29th May, 1945.

Major P. V. Gharpure carried out the post-mortem examination and reported as follows:—

'The body was that of a European male, consistent with an age of 45 years. There was very marked emaciation. Rigor mortis absent. Post-mortem changes had set in.

Cranial cavity.—The skull cap was thick and the brain oedematous. In the floor of the right lateral ventricle a cellular growth bulging into the anterior horn, about 2 cm. in diameter, was present. No other lesions found.

Thoracic cavity.—**Left lung:** Hypostatic pneumonia and congestion of terminal type detected. The lung was rather voluminous with emphysematous bullae. There was thick purulent material in the bronchi which were widely dilated. There were no adhesions and no enlargement of lymph nodes.

Right lung: There was pleural adhesion from the base upwards. The apex was fixed and firm to the touch. A quantity of fluid was contained in the pleural pockets, caused by the adhesions. A tumour about the size of a cricket ball could now be seen involving the right apex and extending upwards to the root of the neck. It had eroded the first, second, and third ribs and caused pathological fractures in the first and second ribs. False capsulation was noted at the upper end. The tumour infiltrated under the fascia of the sixth and seventh cervical and first thoracic vertebrae, causing erosion of the bodies. On section the tumour mass showed a honeycombed appearance of conglomerate suppurating foci and was very soft and friable. The mass above the apex, though fixed, appeared distinct, its cut surface lobulated and soft, dissimilar to that within the lung.

The tumour was mostly in a necrotic state and on pressure a whitish liquid resembling pus oozed out.

Heart was small and pale brown in colour. No valvular or aortic lesions present.

Abdominal cavity: No fluid in the peritoneal cavity. Subcutaneous and tissue fat completely absent. Liver, spleen, pancreas, kidneys, suprarenals, prostate and lymph nodes: N.A.D.'

Dr. R. G. Dhaygude, lately Professor of Pathology, G. S. Medical College, Bombay, very

kindly examined the section of the tumour and sent the following report:—

'The neoplasm is very cellular and extremely pleomorphic. The neoplastic cells vary markedly in size; the smallest are just a little larger than the lymphocyte, the largest (the tumour giant cells with several nuclei) about 30 to 50 times this cell. This marked variation is also seen in the shape of the cells: the majority are spheroidal, some almost round while others appear drawn out, elongated and spindle-shaped; the tumour giant cells are the most irregular in this respect. The cells possess a pale eosinophilic vacuolated cytoplasm and their nuclei are large oval and hyperchromatic. In only some of the nuclei dense basophilic nucleoli can be made out. Mitotic figures, both typical and atypical, are present in conspicuous numbers suggesting rapid growth. The cells are arranged in small and large alveolar groups separated by strands of stroma, which consists of well-formed collagen fibres forming narrow and broad bands to enclose the cell groups. Only a sprinkling of mononuclears can be made out here and there in the stromal tissue. There is no marked vascularity. Areas of degeneration and necrosis are quite conspicuous, affecting mainly the centre of the large cell groups. The histological features suggest the diagnosis of anaplastic carcinoma arising from glandular epithelium' (see figures 4 and 5, plate XXXII).

I am grateful to Major Gharpure for the post-mortem report, Dr. Dhaygude for examining the histological section and microphotographs and to the D.M.S. in India for the permission to report the case.

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A CASE OF PULMONARY AMOEBIASIS

By S. R. SEN GUPTA, L.M.F.

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I WAS much interested in the article on 'Pulmonary amoebiasis' by Chaudhuri and Rai Chaudhuri (*I.M.G.*, February 1946) and in view of their statement that 'clinical recognition of this condition is rarely reported' wish to report the following case, although the diagnosis happened to be purely accidental.

A Hindu male, aged 40 years, was admitted into the hospital on 23rd March, 1946, with general weakness, steady loss of weight, cough with expectoration (sometimes with a trace of blood) along with evening rise of temperature for three months.

On examination: pulse 106 p.m.; temperature 98°F. in the axilla; respiration 30 p.m.; weight 74 pounds. The patient looked very emaciated and had a very poor general physical build. There were râles on the right apical area and breath sounds were diminished on the left side. Percussion note was impaired on both sides. Liver and spleen were palpable below the costal margins.

Clinically the case was diagnosed to be bilateral pulmonary tuberculosis and treatment with gold and calcium was given though repeated sputum examinations failed to demonstrate tubercle bacilli. On 12th April, 1946, the

patient left the hospital as there was no improvement in his condition, but returned on 1st May with complaints of acute pain in the hepatic area along with exacerbation of all previous symptoms.

On admission, liver was painful, tender and enlarged 3 fingers below the costal margin in the mid-clavicular line, upper border of the liver being at the 3rd space. The skin over the hepatic area was red, hot and oedematous. Temperature 101°F., pulse 136 p.m., respiration 45 p.m. Stool showed cysts of *E. histolytica*, and a provisional diagnosis of liver abscess was made. Although this condition was superimposed its emergency necessitated the immediate institution of treatment with emetine hydrochloride $\frac{1}{2}$ grain daily. On the fifth day the temperature touched normal and remained so till the patient was discharged. After about 6 grains of emetine his liver condition subsided along with dramatic disappearance of all the abnormal signs and symptoms of the respiratory system. The sputum was negative for *E. histolytica*. The patient was discharged on 24th May, with much improvement in his general condition and a gain of 7 pounds in weight.

Therapeutic Notes

NOTES ON SOME REMEDIES

IV. THIOURACIL

By R. N. CHAUDHURI, M.B., M.R.C.P. (Edin.),
T.D.D. (Wales), F.S.M.F.

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Medicine, Calcutta*

THE discovery of the action of thiouracil in thyrotoxicosis is the result of alert observation and quick recognition of the significance of certain observed facts. Mackenzie *et al.* (1941) were studying the effect of sulphaguandine as an intestinal disinfectant and came to investigate its toxicity to the rat. They noted that animals dying after sulphaguandine showed goitres which on microscopical section were found to be due to hyperplasia and were practically free from colloid. The same effect was produced more or less by other sulpha drugs such as sulphadiazine and sulphapyridine, and Richter and Clisby (1942) showed that other sulphur compounds, notably thiourea and its derivative, thiouracil, had a well-marked goitrogenic effect. Kennedy (1942) and his colleagues who were investigating the action of rape seed in rat thyroid found the causative agent in allyl-thiourea. These discoveries led to a study of the mode of action of these thio compounds, and the investigations that followed revealed that they inhibit the physiological activity of the thyroid gland and produce the somewhat odd

combination of hypothyroidism and thyroid hyperplasia. This is interpreted as meaning that the thyroid gland is not producing sufficient hormone, thyroxine, for the needs of the body and is being stimulated to hyperplasia to remedy this deficiency. The cause of the hypothyroidism was at first obscure, it could not be due to any neutralizing action of thiourea on the hormone for it is abolished by the coincident administration of thyroxine. It was eventually thought, and this was supported by experimental evidence, that the action of thiourea is to prevent the synthesis of the thyroid hormone and that the lack of this hormone is the cause of hypothyroidism. In response to this condition the pituitary gland is stimulated to increase its thyrotropic activity and in turn the thyroid gland becomes hyperplastic, but is unable to relieve the hypothyroid condition owing to blocking of the thyroxine elaborating mechanism. It was Astwood (1943) who suggested and introduced with beneficial results the clinical use of thiourea and thiouracil in hyperthyroidism, a toxæmic state caused by excessive secretion of thyroxine, and since then many confirmatory reports have been published in England and America.

Method and Results of Treatment

Thiouracil, being much less toxic, has now replaced thiourea, though the action of the two preparations is similar. Of late, another derivative, 4-methyl thiouracil, is being used, it is more easily manufactured and is said to be less toxic and give more rapid control of the signs and symptoms. The aim of treatment is to decrease the synthesis of thyroxine to a normal level but not below it, so that the pituitary will not be stimulated to produce the indirect effect of thyroid hyperplasia. The original dose (1 gm.) has now been reduced, for with it toxic effects were frequent. For initial treatment the dose of either drug is usually 200 mg. given by mouth three times a day. Since thiouracil is rapidly absorbed and excreted, the present tendency is to spread the single doses over the day, e.g. to give 6 doses each of 100 mg. in 24 hours. There is a latent period of one to two weeks before the drug comes to action; this is because it has no power to neutralize the thyroxine already formed in the body. This latent period is prolonged by some weeks in patients previously treated with iodine, although iodine given after thiouracil has no such delaying effect. Leys (1945) found the latent period also longer in the chronic cases, but chronicity did not prevent subsequent rapid progress. According to Himsworth (1944) the first change noted is the disappearance of the skin flush, while the last is a fall in pulse rate. The patient feels a sense of well-being, the tremor and palpitation subside, the weight increases, the basal metabolic rate falls and the blood cholesterol rises. The maximum effect is gradually attained in about four weeks. The effect on eye signs is however

not so striking; stare and lid retraction may diminish, but exophthalmos is not appreciably affected, although Wilson (1946) found it considerably reduced in a few patients with recent history. In most cases there is no noticeable reduction in the size of the thyroid gland, indeed it actually increases in size in some cases. As long as the drug is continued, the improvement persists but on its omission the signs of thyrotoxicosis return but disappear again with the resumption of treatment. It is therefore necessary to give a maintenance dose, the principle being to give the smallest dose that would prevent remissions. So when a satisfactory gain in body weight has been attained, i.e. in 3 to 4 weeks time, the dose is reduced to 50 to 100 mg. a day though occasionally a little higher dose may be necessary. Here also it is better to give suitably divided doses per day than only one. Most patients can go back to work in 3 months. Some have remained well up to one year without the drug, but the present evidence is strongly in favour of continuing the administration of thiouracil in small maintenance doses without interruption.

Cases of primary hyperthyroidism, toxic adenoma and recurrent thyrotoxicosis after thyroidectomy all respond to the drug though in varying degree. There is no uniformity in the rate of improvement and the time required for response varies considerably from case to case. Some clinicians have obtained more striking results in definitely toxic goitre than in milder cases, but it should be remembered that the symptoms of tachycardia, tremor, loss of weight and nervousness may be due to other factors than goitre, neurosis in particular, and Cookson (1945) even goes so far as to suggest that if thiouracil has no effect they are probably not due to the goitre. A small proportion of cases prove resistant to treatment but, as Dunlop and Hill (Dunlop *et al.*, 1946) point out, a patient should certainly not be labelled drug resistant simply on account of the persistence of tachycardia and high pulse pressure during the first few weeks of treatment; it may take a long time before these features of thyrotoxicosis are abolished by thiouracil. Still the possibility of some drug resistance should be remembered when patients resume treatment after discontinuance of the drug.

Thiouracil has no effect on anxiety neurosis sometimes associated with thyrotoxicosis. On the other hand it has been found effective in controlling thyrotoxic auricular fibrillation especially when it is of recent origin, but the normal rhythm is not always restored. Cases are on record showing its good effect in early left ventricular failure. Diabetes is no contra-indication to its use.

Toxic Effects

Regarded at first as relatively innocuous, thiouracil has during these three years of its

discovery grown a long list of toxic reactions but with experience the list tends to become shorter. Toxic manifestations may be due to overdosage or to idiosyncrasy. Gross overdosage causes early enlargement of the goitre which may produce pressure symptoms. Toxic symptoms from chronic slight overdosage are insidious and appear later, and are recognized by coldness, fatigue, depression and a bloated appearance. But owing to the reduction of the dosage these effects are seldom seen nowadays. Those that are seen at present are more often due to idiosyncrasy and appear in the second week or later during the period of initial treatment and occasionally during the maintenance period. They usually disappear when the drug is withdrawn. The commonest manifestations are skin rashes of various types, adenitis, joint pains, headaches, oedema of feet and gastrointestinal symptoms including nausea, vomiting, abdominal pain and diarrhoea. A febrile reaction develops about the end of the first week with or without enlarged spleen. Jaundice has been reported a few times and occasionally there has been complete loss of taste. But its most important effect is on the blood. Thiouracil does not usually depress the white blood count as is thought by some, and in assessing its effect it should be noted that slight leucopenia is usual in untreated toxic goitre. Nevertheless, the drug may lead to definite leucopenia and neutropenia in some cases. Neutropenia can develop into agranulocytosis if the drug is continued but usually returns to normal if it is omitted or given in reduced dosage for a few days. Two surveys made in the U.S.A. by Moore (1946) and by Van Winkle *et al.* (1946) respectively covering 1,091 and 5,745 patients treated with thiouracil showed that agranulocytosis occurred in a little more than 2 per cent of cases, and caused death in 0.4 per cent; more than 70 per cent of these cases of agranulocytosis developed within the first eight weeks of treatment. No relation could be discovered between the incidence and dosage. Other toxic effects were found in about 10 per cent, the commonest being fever, glandular enlargement and various types of rash. Reports on more recent series of cases are encouraging and indicate fewer toxic signs and symptoms. However, agranulocytosis is still a definite risk, and the drug should not be used where there are no facilities for frequent white cell counts and if the white blood count falls below 3,000 the drug should be stopped. And it is also important to instruct the patient to report development of any fresh symptoms, a sore throat in particular, for agranulocytosis often comes on suddenly without warning. For prevention various remedies have been suggested besides keeping to a minimum effective dose: folic acid, proteolysed liver, various members of the vitamin B complex and intravenous injection of pyridoxine hydrochloride.

Pregnancy is no contra-indication to the use of thiouracil so far as the mother is concerned,

but Goldsmith *et al.* (1945) found that its administration to pregnant rats resulted in activation and hyperplasia of the thyroid gland and retarded growth of the offspring. These effects were however transient and disappeared when the young rats ceased to imbibe the milk of thiouracil-treated mothers. Eaton (1945) reports the case of a woman who was on this drug during pregnancy. The child after birth had an enlarged thyroid gland but was normal in all other respects. At the age of three months the gland was no longer apparent and growth had been normal. Davis and Forbes (1945) found post-mortem enlargement and hyperplasia of the gland in a foetus six months old, the mother having been on thiouracil for nearly a year. These findings are of practical importance. Though the effects appear to be transient, the administration of thiouracil to pregnant women calls for caution and Eaton suggests that it should be replaced by iodine some weeks before delivery.

Advantages and Disadvantages

The cause of exophthalmic goitre is still unknown and treatment has hitherto been directed towards reducing the circulating thyroxine, whether it be by surgery, by x-rays or by drugs such as iodine and thiouracil. It is too early to say what the ultimate effect of thiouracil may be. According to Marine's researches (1935) long-continued hyperplasia of the thyroid eventually gives way to atrophy of the gland, and if we can tide the patient over with thiouracil until this occurs, the state of thyrotoxicosis may be cured. There seems no reason to suppose that its careful use will result in such atrophy as will cause undesirable hypothyroidism. On the other hand, it may be that the disease involves a vicious circle of stimulation of the thyroid by the pituitary and stimulation of the pituitary by the thyroxine and that thiouracil by breaking the circle helps the thyroid to return to a relatively normal state and a cure is thereby obtained. Meanwhile, whatever be the mechanism and the end result, its use must be discriminating and the following observations may be of help to practitioners in applying it clinically.

Thiouracil has proved very effective in the treatment of thyrotoxicosis, though under certain conditions it may fail. It has two drawbacks: one is its toxicity, but there are grounds for believing that with increasing experience these effects will be further reduced or become insignificant. Its potential dangers need not deter any one using it so long as he observes the precautions already indicated. The second drawback is the necessity for continuing the maintenance dose for an indefinite period, and this is troublesome to both the patient and his medical attendant. Surgery, on the other hand, is the quickest way to ensure recovery from thyrotoxicosis. The operation of thyroidectomy has

attained a high degree of perfection in expert hands. Patients suffering from pressure symptoms will require surgical treatment on account of the tendency of the drug in some cases to cause enlargement of the gland. Surgery should also be the choice for patients with a retro-sternal goitre or with pronounced enlargement of the gland, and for those few who are drug resistant or show persistent reactions to it. Apart from these considerations, thiouracil may be tried first in most cases. It is more potent and more permanent in action than iodine, but as its effects are not immediately seen, iodine should be required when rapid action is required as in thyroid crisis. In the elderly with cardiovascular complications and in children thiouracil has advantages over operation. It is the obvious choice for those who are averse to operation. There are some patients unsuitable for thyroidectomy or who relapse after such treatment: they usually respond well to thiouracil. It is also very important in pre-operative treatment as it can be relied upon to detoxicate the patient and obviate the post-thyroidectomy crisis due to the liberation at operation of hormone stored in the gland. On the other hand, it causes the gland more vascular, causing troublesome bleeding during operation, this can be avoided by reverting to iodine a few days before the operation.

To summarize we have in thiouracil a weapon almost as effective as surgical treatment in selected cases. There are risks, and these should be realized so that treatment should not be haphazard and uncontrolled.

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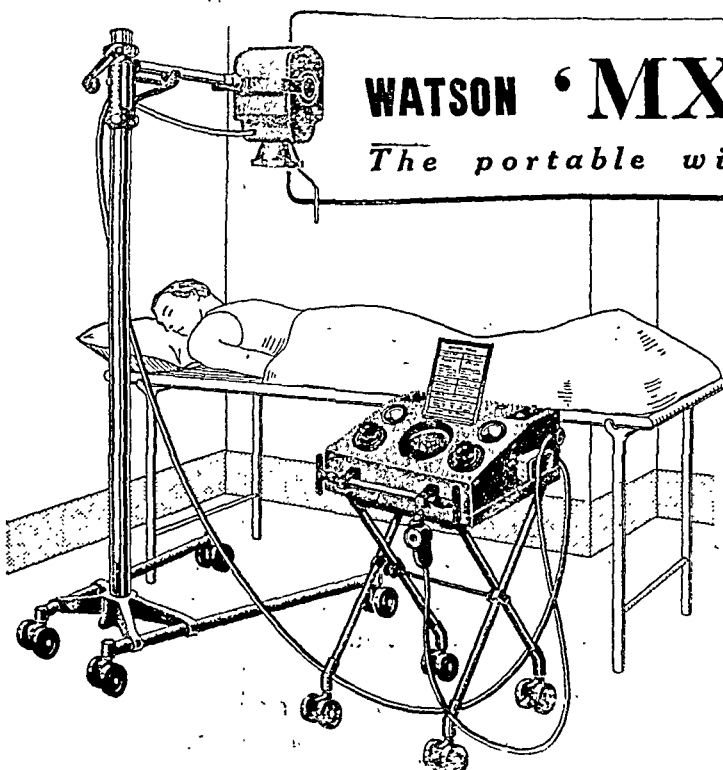
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Indian Medical Gazette

DECEMBER

ANTIBIOTICS

THESE substances are elaborated by micro-organisms against other micro-organisms of different species probably as a means of defence in the struggle for existence in the limited living space of this planet. Through their agency are obtained results which are diametrically opposed to what occurs in symbiosis which guarantees mutual benefits to two species living together.

Substances like quinine and emetine elaborated by organisms of an order higher than that of micro-organisms, although antagonistic to micro-organisms and elaborated by biological units, are not called antibiotics. Nor are hormones called antibiotics: they are 'biologics'.

Towards the close of the last century *Pseudomonas pyocyanea* (*Bacillus pyocyaneus*) was the first bacterium to be studied as a producer of antibiotics. Many substances like pyocyanase, pyocyanine and α hydroxyphenazine were isolated (Wilson and Miles, 1946).

Although antibiotic tendencies of moulds were known since Pasteur's time, *Penicillium notatum* (a native of Norway) was first studied by Fleming in London in 1929 (Fleming, 1929). The filtrate of the peptone broth medium in which it was grown was called

Penicillin

During World War II, Florey and his colleagues at Oxford isolated this active antibiotic in a more or less pure state.

The substance is an acid. Several varieties exist. All are dipeptides of the molecular formula $C_9H_{11}O_4N_2SR$, the only difference being the constitution of the radical R. Four are well known:—

Penicillin	I or F
"	II or G
"	III or X
"	IV or K

The chemistry of penicillin is still subject to the Official Secrets Act (The Pharmaceutical Society of Great Britain, 1946). The ban is likely to be lifted in the near future and a synthetic manufacture may be possible. As a matter of fact such a manufacture appears to have been considered during the war. The increased production from bacteriological procedures, however, was found possible and adequate to meet the needs of the Services.

The substance as supplied for use in the form of a yellowish crystalline powder is either a sodium or a calcium salt. For intrathecal injection the calcium salt is preferred.

The purest solid preparations of penicillin so far described contain about 1,650 Oxford units per milligram. Staphylococci are inhibited *in*

vitro by concentration of penicillin equivalent to 0.01 to 0.02 units per c.c. (Anderson, 1946). For estimating potency a newly made lot is compared with a standard preparation.

The instability of the product is not such a problem as it was stated to be last year. Under precautions in transport and storage the salts retain their potency long enough. Recently, many preparations have received the stamp of B.P. and many more are standard pharmaceutical preparations of known worth. They include injections (watery and oily), lotions, suspensions, emulsions, ointments, mixtures (for oral use), capsules, dusting powders, eye and nasal drops, lozenges, pastilles, sprays, snuffs, lamellæ, suppositories, pessaries and chewing wafers (named in the order of introduction). The simple fact that so many preparations have been made shows that the antibiotic when not given by the needle is not so inert as it was supposed to be. The dose and mode of administration are bound to be revised now that cheaper and ampler supplies are available.

Even the list of organisms sensitive to penicillin may need a revision. So far the majority of organisms which are known to be sensitive to penicillin are 'gram-positive, namely, *staphylococcus*, *streptococcus*, *pneumococcus*, *C. diphtheria*, *B. anthracis*, *actinomyces*, *Cl. welchii*, *Cl. oedematiens* and other clostridia. The sensitive gram-negative organisms are the gonococcus, meningococcus and *Micrococcus catarrhalis*. The other gram-negative pathogens are not affected by penicillin nor are gram-negative saprophytes, yeasts or moulds. The tubercle bacillus is not sensitive to penicillin. The activity of penicillin is not affected by the presence of serum, blood or pus nor by the number of organisms present'.

Two warnings, however, are essential in India where the transport and storage facilities are likely to be inferior to those in Europe and America: (1) The ready-made preparation should be made locally and by firms of repute. (2) The potency of the salt to be used for injection should be tested before use. For this purpose perhaps a hæmolytic test (Paterson, 1946) will be specially apt. Red blood cells inoculated with hæmolytic streptococcus are saved from hæmolysis by penicillin. The leucocytes must be removed by filtering through cotton-wool or the blood must be three days old.

Because of its lack of toxicity to the patient penicillin stands unique in therapeutics. Reactions occasionally seen are allergic and due to impurities. They may be either ignored or another brand of the drug used to continue the treatment. Fastness to the drug in the micro-organisms, due to an inadequate dose, does not develop. Any resistance encountered can nearly always be overcome by a bigger dose. Instances of the recurrence of a disease after stopping the treatment are known. They are not many.

Some 30 preparations like penicillin have been made from moulds, bacteria and vegetables

(Anderson, *loc. cit.*). They are far inferior to penicillin with the exception of

Streptomycin

which is derived from *Streptomyces griseus*, one of the soil organisms, the actinomycetes. It is an organic base. It inhibits the growth of gram-negative as well as gram-positive organisms, but is more active against *Pr. vulgaris* and *Ps. aeruginosa* among the former and against *B. mycoides* and *M. tuberculosis* among the latter. It is also bacteriostatic to *E. typhosa*, *Sal. schottmulleri*, *Br. abortus*, *H. influenza*, *H. pertussis*, *Serratia marcescens*, *B. subtilis*, *Staph. aureus* and *Cl. butylicum*. Streptomycin is poorly absorbed from the intestine but is not destroyed and so may be useful for controlling intestinal infections. In man it is rapidly absorbed and excreted in the urine after parenteral administration, but therapeutic levels can be maintained in the blood and urine more easily than with penicillin. It has low toxicity for animals. Preliminary trials indicate that it may be of therapeutic use against typhoid fever and human tuberculosis. If these claims are substantiated streptomycin is likely to be as valuable as penicillin.

Streptomycin appears to be particularly effective in suppressing infection in the urinary tract (*B.M.J.*, 1946).

The drug is not yet available for extensive trials.

Not covered by the original definition yet studied with the antibiotics is

Allicin

from garlic, *Allium sativum*, which is active against gram-positive or gram-negative organisms (Anderson, *loc. cit.*). It has not been studied in detail although garlic is used in indigenous medicine and used extensively in Oriental cooking as a flavouring agent. Certain sections of the Hindu community avoid the agent.

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Special Article

FIRESIDE FANTASIES

By S. D. S. GREVAL, B.Sc. (Punjab), M.D., Ch.B., D.P.H. (Liverpool)

13/2, Ballygunge Park Road, Ballygunge, Calcutta

1. Immunized vegetables and fruits

THAT one virus disease of a plant protects it against another closely allied disease (cf. cowpox and smallpox in man) is known; that there are rust and smut-resisting strains of cereals is also known; what is not known is the as-yet-to-be investigated humoral system of the plant, in other words, the immunology, popularly known as serology, of the plant. It is more than probable that such a system exists. It should be possible to produce in plant tissue antibodies which will resist viruses, bacteria, protozoa, worms and even arthropods. These antibodies could be harvested in and with the fruit and administered to the patient suffering from the lodgment of one of the parasites enumerated.

Means could easily be devised of introducing the parasite or its essence. Hollow stems are like veins. Even hard stems form tannic and gallic acids in response to the stings of insects: they may form antibodies also.

The plant could be selected with regard to the suitability of response, the dosage of the

antibodies and the keeping power of the fruit. A cucumber would be excellent for curing acute fevers locally. A melon could be sent from Kabul to Calcutta comparatively easily. Dates grown and packed in Iraq with no better attention than is given to them at present, and despatched by the cheapest route to all parts of the planet, will be available always for more chronic maladies needing many small doses.

Parasitization of man by the disease producing members of the vegetable kingdom specially calls for the mediations of plants. Probably the parasitism arose from the upset of the ecological balance during the development of civilization. Something similar is known in trypanosomiasis of man. Tribes of fungus having been deprived of *Phytus susceptible*, on which they lived with or without causing damage, at some stage of the latter's growth or decay, in the marshes of Bengal, might have run amok and attacked man as ringworm, tuberculosis or leprosy. They can be made to fight *Phytus semisuscepticus* and the antibodies gathered in the concentrated 'phytoserum' of the fruit. Plants would probably prefer fighting their own kind to fighting animals, if given facilities. All living things do so.

Flagellates are known to live in some plants which have a milky juice. Do they start kala-azar in man, when disturbed?

2. *The old and the new in sanitation*

Under the old system of village sanitation in India when a case of cholera happened to contaminate a pond in the early stages of the attack he also inoculated it with the appropriate bacteriophage a few hours later. Now he only contaminates it. Further, the natural phage may be much more effective in checking epidemics than the test tube grown phage.

The phage, by the way, may be one of two things: it may be either a parasite of the parasite (a smaller bug feeding on a small bug) or a cyclostage arising spontaneously in the life cycle of a bacterial species and destroying most of the organisms so that the fittest may dominate the bacterial world (like a drastic party purge, or like the fire which an old phoenix lighted with a song in a funeral pyre built by himself to immolate his own body so that from the ashes might arise a younger bird of lustier songs). Whatever the bacteriophage is, it destroys most of the bacteria it is found in association with.

The Ganges water collected at Hardwar has the reputation of resisting rotting. Probably phages derived from millions of pilgrims provide the mechanism concerned.

3. *Living with the live stock*

Calcutta breeds *Anopheles stephensi* very well, yet had before World War II very little malaria. The majority of the anopheles caught from human habitations in the city were found to have fed on blood of cattle, not of man. That was the secret of the low incidence of malaria. The live stock shielded man. The cattle no longer roam in the streets and malaria has increased.

In a thin zone of the crust of the earth, which divides geology from archæology, are recorded the daily lives, triumphs and tribulations of the cave dwellers who lived with their live stock. They were never wiped out as suddenly and dramatically as were some of the latter day populations. The Mayas of the pre-Columbian American fame in art and mathematics were a highly civilized race. They were wiped out almost overnight. Did they succumb to successive epidemics of malaria consequent on abnormally high rainfalls? Had they in their zeal for æsthetics and tidiness segregated their live stock unduly? This seems to be very likely in the light of the fact that they stand apart from the rest of humanity in developing a civilization which invented a sign for the zero and devised a calendar but completely ignored the art and science of war. They relied on their civic sense for possession of property, not on proximity, and might easily have left the cattle in the pastures.

Item 3 is no more of a fantasy than of a proposition which can be developed in the interest of public health. The mere æsthetic effect of the nearness of the live stock must be differentiated from the real insanitation which

may also be encountered. The latter can be remedied. The æsthetic effect being a question of taste, usually acquired, mostly by imitation, is not a public health problem.

Incidentally, the inconvenience caused to youthful dashing motorists of the days of peace and plenty of the late thirties by the animals in Central Avenue, Calcutta, was a blessing in disguise. It controlled excessive speed and saved many a life and limb.

Medical News

MEASURES AGAINST YELLOW FEVER

NEW INDIAN AIRCRAFT (PUBLIC HEALTH) RULES, 1946

WITH the growth in civil aviation it has been found necessary to take stringent measures to prevent the introduction of yellow fever into India from the endemic areas, especially of Africa.

The Government of India have, from time to time, made amendments in the Indian Aircraft (Public Health) Rules, 1940, and have now issued the Indian Aircraft (Public Health) Rules, 1946, incorporating all these and certain other amendments.

Under the new rules all aircraft coming from the West are required at present to land at Karachi. On arrival the aircraft and cargo may be disinfected and all persons on board are to be medically examined either before disembarkation, or under such arrangements as may be made by the Airport Health Officer to reduce the risk of spread of infection to a minimum.

The new rules also make some changes in the period of validity of yellow fever inoculation certificates.

COLLEGE OF PHYSICIANS AND SURGEONS OF BOMBAY

THE Council of the College of Physicians and Surgeons of Bombay at a Special Meeting held recently has decided that no students should be admitted for the L.C.P.S. Course into an affiliated Institution after December 1948.

FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students were declared to have passed the L.T.M. Examinations held on the 20th September, 1946, and subsequent days:—

Passed

(Arranged in alphabetical order)

1. Arora, Ram Dass.
2. Bhadra, Abinash Chandra.
3. Bhattacharjee, Rakhal Chandra.
4. Chakravarty, Sailesh Chandra.
5. Chanda, Bejoy Kumar.
6. Das, Debesh Chandra.
7. Das, Nripendra Chandra.
8. De, Hari Pada.
9. Dutta Roy, Susil Kanta.
10. Goswami, Nanda Gopal.
11. Gupta, Beni Madhava.
12. Kanak Prasad.
13. Khanna, Kesho Ram.
14. Kirloskar, Hemkanta Ramchandra.
15. Likhitar, Madhab Bapuji.
16. Mathur, Jeewan Lal.
17. Mehta, Jai Dayal.
18. Mozumdar, Satyendra Prasad.
19. Mukherjee, Hari Gopal.
20. Paul, Gouranga Pada.

21. Paul, Mrityunjoy.
22. Paul, Sreemohan.
23. Rathi, Badrinath Tulsiram.
24. Shah, Suresh Chandra Chimanlal.
25. Shahade, Bindumadhav Shripad.
26. Sharma, Chait Ram.
27. Singh, Lokeshwar Prosad.
28. Singh, Man Mohan.
29. Sur, Mohan Lal.
30. Susheela, Prabhudas Samuel.
31. Thaman, Jagjit Ram.

CURARE TO AID ANÆSTHETICS : DOCTOR'S SELF-EXPERIMENT

(Abstracted from a Release dated June 24, 1946, by the Press Information Bureau, Government of India, New Delhi.)

A *Star* columnist writes that Dr. Frederick Prescott, Director of Clinical Research at Wellcome Research Institution, is to see whether curare, a deadly poison with which South American Indians tip their darts and arrows, could be used to make anæsthetics safer in operations.

His chief collaborators were Dr. Geoffrey Organe and Dr. Stanley Rowbotham, two of the most skilled anæsthetists in England. They described Dr. Prescott's experiences as terrifying. An injection of curare paralysed him; he was unable to speak, swallow, cough or move.

When paralysis stopped his breathing, he was revived by artificial respiration. In six hours he had recovered and there have been no after effects.

All Dr. Prescott would say was : 'I knew unconsciousness was coming over me, but I was unable to give any sign. I tried and failed. We have learned a great deal. Properly administered, curare and its derivatives will prove a great aid in anæsthetics and eliminate many post-operative complications'.

This is not the first time that Dr. Prescott has risked death. Some time ago, to test out the drug, he gave himself a large dose of methedrine without consulting anyone. His blood pressure shot up to over 200 and in 24 hours his condition became critical. Then he was in hospital for nearly a week. As a result of his self-experiment doctors are now able to treat blood pressure with sure knowledge they had not previously obtained.

SITES FOR INTRAMUSCULAR INJECTION

IN answer to a query, the following directions are given in the *British Medical Journal* (27th July, 1946, vol. ii, p. 147) regarding the sites for intramuscular injection.

Buttock.—Injections are often made close to the tuberosity of the ischium into what is thought to be the thickest part of the gluteus maximus muscle. The curve of this part of the buttock is produced largely by fat, there is less thickness of muscle than elsewhere in the buttock, and the course of the great sciatic nerve runs dangerously close to the site of injection. The accompanying sketch (figure 1) shows that in relation to the great sciatic nerve the safe area of the buttock lies above a line joining the top of the greater trochanter of the femur to the third sacral spine. The latter usually lies deep to the top of the natal cleft, but its position can be checked by finding the second sacral spine at the level of the line joining the two posterior superior iliac spines. It is a good plan to mark this safety line on the skin with dye or a skin pencil when injections have to be given by assistants who have not had much experience of the technique. Just above the junction of the middle and posterior thirds of this line is the optimum spot.

Thigh.—Intramuscular injections may be given with safety into the lateral aspect of the upper two-thirds of the thigh, as all the important structures lie medial or posterior to the femur and out of harm's way.

Injection here is usually more painful than in the buttock.

Deltoid region.—Although injections in this region can safely be made by an experienced person, it is not a suitable site for routine use when deep injection is

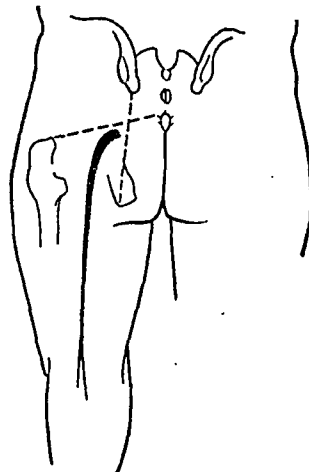


Fig. 1.

required. Near its insertion the deltoid muscle becomes too thin for an injection to be made without giving an unnecessary amount of pain. In the upper and more fleshy part of the muscle there is a risk of damaging the circumflex nerve, or of making the injection into the shoulder joint. Distal to the deltoid insertion the radial nerve is in danger.

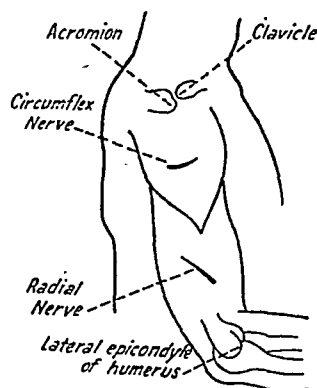


Fig. 2.

Interscapular region.—This site would be chosen for injection only when circumstances forbade the use of the more suitable areas. The injection should be made into the sacrospinalis (erector spinæ) muscle. The risks of going too far laterally and entering the chest, or too far medially and entering the subarachnoid space may easily be avoided by the expert, but must not be run by those with little knowledge or experience. Furthermore, even in expert hands, an injection given in this area must surely be more uncomfortable for the patient than injections made in almost any other part of the body.

In conclusion it may be said that experience shows the safe area of the buttock to be far and away the best site in the body for intramuscular injections.

UNIVERSITY OF MADRAS

COUNCIL OF POST-GRADUATE MEDICAL EDUCATION

A COURSE of Post-Graduate lectures in (a) Medicine, (b) Surgery, (c) Obstetrics and Gynaecology, (d) Ophthalmology, and (e) Oto-Laryngology will be held from

January to March. Each of these subjects will comprise 20 lectures, more particularly intended for those preparing for the higher degrees and diplomas in medicine.

A short refresher course in modern methods of treatment and diagnosis in (a) Medicine, (b) Surgery, (c) Obstetrics and Gynaecology, and (d) Venereal Diseases will also be held during January to March 1947. The course in each subject will extend over a period of 2 weeks, except in venereal diseases which will extend over a period of one week, and will be held in the city hospitals.

The Post-Graduate and Refresher Courses are open to registered medical practitioners of the allopathic system. Particulars regarding the courses can be had from the Secretary to the Council of Post-Graduate Medical Education, University Buildings, Chepauk, Madras.

THE OVERSEAS POST-GRADUATE MEDICAL JOURNAL

WE have received the first number of a new quarterly publication, *The Overseas Post-Graduate Medical Journal*, edited by F. Croxon Deller. It is designed to be of value to post-graduates all over the world, studying for higher degrees in their profession. The journal is published by 'The Fellowship of Post-Graduate Medicine', 1, Wimpole Street, London, W.1, the annual subscription being £1-10-0.

BHORE COMMITTEE'S RECOMMENDATIONS : ACTION TAKEN BY CENTRAL GOVERNMENT

FIFTY-FOUR students have been selected for advanced training abroad in health services and arrangements for placing them in institutions in U.K. and U.S.A. are in progress.

This information was given in reply to a written question in the Central Assembly as to what action the Central Government proposed to take on the principal recommendations of the Bhore Committee Report.

The House was further informed that candidates were also being selected for higher dental training and training in industrial hygiene and nutrition. The staff of the All-India Institute of Hygiene and Public Health in Calcutta has been increased to provide for 60 public health students a year and other specialized courses. The Bhore Committee's recommendation for the establishment of an All-India Medical Institute has been accepted on principle and a committee will be appointed to advise the Government on the steps to be taken to establish the institution.

A Bureau of Standards for medical institutions has been set up, which will supply model type designs for hospitals to Provincial Governments and serve generally as a clearing house for information relating to the design and equipment of medical institutions.

SYPHILIS IN INDIA

(Abstracted from the *Urologic and Cutaneous Review*, June 1946, p. 379)

THE history of syphilis in India can be traced back to the oldest times. The Ayurveda, or the medical precepts of the venerable Dhanvantri collected by his disciple, Sushruta, contains several curious passages which show that the disease was a well known one in old India. The word used at that time probably was Upadansa, and this in Sanskrit means the syphilitic virus. The book not only gives the description of the disease, but also the therapeutic measures employed. According to Hessler, Ayurveda dates back at least one thousand years B.C. as the name Sushruta was celebrated among the Hindus many centuries before the Christian era.

Under the heading *Nidabasthana* there is a chapter which treats of ulcer. Here the author begins by explaining that these ulcers are caused by bad nutrition, or by contact with a woman in the sexual act. The description runs as follows :

'Lingarsas (figwarts or condylomatous growths about the genitals): The deranged and aggravated *Vayu* finding lodgment in the genitals, vitiates the local flesh and blood, giving rise to an itching sensation in affected localities. The parts become ulcerated and the ulcers become studded with sprout-like vegetations of warts which exude a kind of slimy, bloody discharge. These growths generally appear on the inner margin, or on the surface of the glans penis in the form of soft, slender vegetations of skin, resembling the hairs of a small brush. These vegetations ultimately tend to destroy the penis and reproductive faculty of the patient.' *Bhagarus*: The deranged *Vayu* of the body lodged in the vaginal regions of a woman, gives rise to similar crops of soft polypi in the passage. They may crop up isolated at the outset, and by coalescing may assume the shape of a mushroom or an umbrella, secreting a flow of slimy, foul-smelling blood.'

'The deranged *Vayu* may further take an upward course, and finding a lodgment in the ears, nose, mouth and eyes, may produce similar warts in these localities. Warts, which crop up inside the cavities of the ears, may bring on earache, dumbness and a foul discharge from those organs, while those cropping up in the eyes will obstruct the movement of the eyelids, giving rise to a pain and local sensation and ultimately destroy the eye sight. Similarly, such growths in the nostrils produce catarrh, excessive sneezing, shortness of breath, headache, nasal speech and the complaint known as *Putinasya*. Such vegetations cropping up in and about the lips, palate and larynx tend to make the speech confused and indistinct. When appearing in the mouth, they impair the faculty of taste, and diseases which affect the cavity of the mouth follow. The excited *Vyana Vayu* united with the aggravated Kapham, produces a kind of hard papillomatous growth on the skin about the anus which are called the *Charmakilas* (Papillomata).'

The text clearly reads like a condensation of the symptoms of the secondary period. The *Vayu* described therein was nothing but a virus which takes its point of departure from the penis where it manifests itself in local itching. From here the text leads us to the upper regions and describes the mucous patches on the mouth, ulcers in the ears, etc. Probably this is the tertiary period with consequent depressed nose and perforation.

Sushruta did not hesitate in calling syphilis a shameful disease and quite correctly described the consequences of it : alopecia, alterations in the nails, papules of the skin, stricture of the anus, etc. Syphilis was certainly well known as a clinical entity in ancient India.

QUININE PRODUCTION

(Abstracted from the *Pharmaceutical Journal*, 24th August, 1946, p. 127)

PRODUCTION of quinine in the Netherlands Indies was actually increased by 16 per cent during the Japanese occupation, states *U.S. Foreign Commerce Weekly*. Output in 1944 totalled 747 tons, compared with 650 tons in 1940. The area planted with cinchona trees declined from 36,062 acres in 1942 to 34,095 acres in 1945. In some areas cinchona was planted at the expense of tea culture. In almost all cases, upkeep and maintenance were entirely adequate.

The Japanese erected two factories for the treatment within the islands of all Netherlands Indies cinchona bark production. They may be of considerable use when production on a large scale is resumed. The Dutch anticipate no difficulty regarding the rehabilitation of quinine production when conditions become stabilized.

Public Health Section

MALNUTRITION IN BENGAL

By J. P. BOSE, M.B., F.C.S. (Lond.)

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Introduction

MALNUTRITION is a term which is not quite easy to define. A review in the literature will show that different workers in the field hold different views about the state of malnutrition and its cause. Most workers however hold the view that malnutrition is not caused by underfeeding alone but by the prolonged use of food in which certain essential constituents of food are either absent or present in insufficient quantities.

Apart from the difficulty in properly defining malnutrition, it appears that it is more difficult to set up a definite cut and dried standard by which the degree of malnutrition could be easily measured.

The state of one's nutrition depends on the total well-being and right functioning of the different systems of the body. Various methods have been adopted for assessing the degrees of malnutrition, one method being what is known as 'Anthropometric measure'. This includes measurements of height (including sitting height) and weight and comparison of these with a chosen standard for the age and sex of the individual. According to some authorities if the weight of the individual falls 10 per cent or more below his average normal weight for his age and height he can be labelled as a case of 'Malnutrition'. Greater reduction of course indicates greater degree of malnutrition. There are other authorities who disagree with this method of assessment and advocate other lines of assessment putting great stress on a thorough and systematic clinical examination by an experienced physician regarding general fitness, endurance, etc. In this method also differences of opinion are bound to occur because no two observers employ the same criteria as the basis of their judgment. There are again other observers who state clearly that the state of nutrition of the human body cannot be judged by artificial and arbitrary method and assessment but evidence should be obtained of the condition of the blood, the skin, subcutaneous fat, the skin tension determined by the water content of the subcutaneous tissues, the condition of the muscles and the condition of the alimentary, circulatory and the nervous systems before any judgment can be pronounced.

Malnutrition in Bengal

Whatever may be the standard adopted by various workers to detect malnutrition it is

generally agreed that there is a good deal of malnutrition in Bengal. According to Sir John Megaw's inquiry on this subject 78 per cent of the people of Bengal are undernourished and suffer from malnutrition due to inadequate and improper diet (Gangulee, 1939). McCarrison at Coonoor, by his striking feeding experiments on albino rats, has also definitely proved that the average Bengali diet is one of the worst and is the cause of malnutrition to the greater part of the Bengali population. McCay also holds the same opinion which is also corroborated by other workers in the field. The consensus of opinion among the different workers is that the marked deficiency of proteins of the proper biological quality as well as that of fats in the Bengali diet is one of the potent causes of such widespread malnutrition in this province. This diet is also extremely poor in the protective nutrients (vitamins, minerals, etc.) which easily makes them an easy prey to diseases caused through malnutrition.

It will thus be evident that even under normal conditions the majority of the Bengal population suffer from malnutrition in various degrees depending on the social and economic conditions of the individual. In the event of some sort of a crisis such as food shortage, famine, etc., these individuals, already on the lowest state of existence, become easy victims of starvation and death.

Such a condition appeared in autumn 1943, when with the outbreak of a famine in Bengal, Calcutta was flooded with destitutes who came to the city and its suburbs in large numbers in search of food. Many of these cases were admitted into the hospital and detailed biochemical and other investigations were done on them and a preliminary paper has already been published (Bose *et al.*, 1946).

Types of Cases

During the investigations it became apparent that clinically two distinct and separate types of cases were discernible and the cases were divided as follows:—

Group A cases of acute starvation.—The history of these cases revealed that there was no underfeeding or malnutrition prior to their real starvation period which was rather acute and which lasted for 3 to 4 weeks.

These were found to be emaciated sometimes to an extreme degree but were generally of the 'dry' type, *viz.*, having no oedema anywhere.

Group B cases of chronic malnutrition.—Most of these cases gave history of poverty, prolonged underfeeding and malnutrition prior to the actual period of starvation. When food shortage became acute they became indiscriminate as regards food intake and did not hesitate even to eat garbage from the street dust-bins.

These were usually of the 'wet type', *viz.*, having widespread œdema all over the body with marked ascites. Most of these subjects were suffering from other intercurrent diseases such as pneumonia, bronchitis, dysentery, malaria, diarrhoea, etc.

Laboratory Findings

Although the division of the starvation cases into groups A and B was made on the history and the physical findings, the subsequent laboratory findings corroborated the clinical classification originally made as will be seen from the marked difference in the results obtained in the two groups of cases. Some of these differences, particularly those with regard to carbohydrate metabolism and serum protein content, were so remarkably clear cut that one could predict as to what group the case belonged on the result of the biochemical findings. A synopsis of the results obtained in the majority of the cases in the above two groups, showing the difference in the laboratory findings, is given below :—

	Group A cases	Group B cases
Blood sugar	Low or normal.	Low
Blood N.P.N.	"	High
" urea N	"	"
" uric acid	High	"
" creatinine	Normal	Normal
" cholesterol	Low	Very low
" phospho lipid	Normal	High
" calcium	Low	Low
" chlorides	"	Normal
Serum protein (total)	Low or normal.	Low
" albumin	Low	Very low
" globulin	Normal or high.	High
Glucose tolerance	Low	Low or normal.
" absorption	Normal	Markedly impaired.
Chloride excretion	Very low	Low
Urea excretion	"	"

Carbohydrate Metabolism

In group A, the majority of the cases showed a definite lowering in carbohydrate tolerance. The initial blood sugar was low in most cases but the blood-sugar curves after a test meal of 50 gm. of glucose usually resembled those seen in cases of diabetes of varying degrees of severity. A detailed inquiry into the cause of this variation in the degree of defect in the carbohydrate utilization of these people revealed that this depended mainly on the degree of starvation; those undergoing short but not acute starvation showed either normal or slightly defective carbohydrate tolerance whereas those undergoing acute starvation gave results resembling those seen in cases of diabetes of moderate or even severe degree.

The group B cases on the other hand gave an entirely different type of results. Here also the initial blood-sugar level was low but the ingestion of 50 or even 100 gm. of glucose made no impression on the blood-sugar level at all. In a few cases in this group, it was found that the blood sugar, after the glucose meal, showed even a further decrease below the initial level at the end of the second and third hours. The reason for this peculiar behaviour of blood sugar after the glucose meal is not clear though we have obtained similar results in anæmia and sprue.

The intravenous method of glucose tolerance test done on these cases however revealed that in many of these cases the utilization of glucose was defective sometimes to a marked degree. It can thus be assumed that the failure of the blood sugar to rise after the glucose meal in these cases was due to impaired absorption from the alimentary tract. It is suggested that malnutrition due to starvation may lead to a condition of the alimentary canal where the power of absorption even of glucose may be partially or even completely lost.

It is thus evident that starvation reduces the blood-sugar level and causes a definite impairment of the glucose utilization and absorption power of the individual.

The typical results obtained in the majority of cases in the above two groups are given below and are represented graphically as well.

Serum Protein

Group A (emaciated cases).—The loss of total protein in blood in this group was not marked but there was a reduction in the albumin fraction, globulin fraction being slightly increased.

Group B (œdematous cases of chronic malnutrition due to long starvation).—The loss of total protein in the majority of this group of cases was marked and in some extremely low values were obtained. The albumin fraction was also markedly decreased whereas the globulin fraction was high.

The fall in serum protein does not, however, represent a uniform and proportionate decrease of its two constituents (albumin and globulin) and herein lies the importance of our findings. A critical survey of our results clearly shows that the albumin fraction of the protein is more or less markedly decreased in most cases, more particularly in the cases of B group, whereas the globulin fraction was usually increased. It is thus evident that the decrease in the total protein content of the blood was due entirely to the diminution of the albumin fraction.

The fact that the albumin fraction of the serum is decreased while the globulin fraction either remains normal or is increased results in a serious alteration of the normal 2:1 albumin/globulin ratio. As a matter of fact, in some of the group B cases where the albumin fraction was markedly decreased and the globulin fraction markedly increased there was an actual reversal of this ratio.

TABLE I

Effect of oral administration of glucose on the blood sugar in cases of groups A and B

	BLOOD SUGAR IN MG. PER 100 C.C.					
	Before giving glucose	½ hour after glucose	1 hour after glucose	1½ hours after glucose	2 hours after glucose	3 hours after glucose
Group A cases ..	63.3	158	198.6	212.3	218	217
Group B cases ..	65	65	65	65	53	45

These results are shown in graph I.

TABLE II

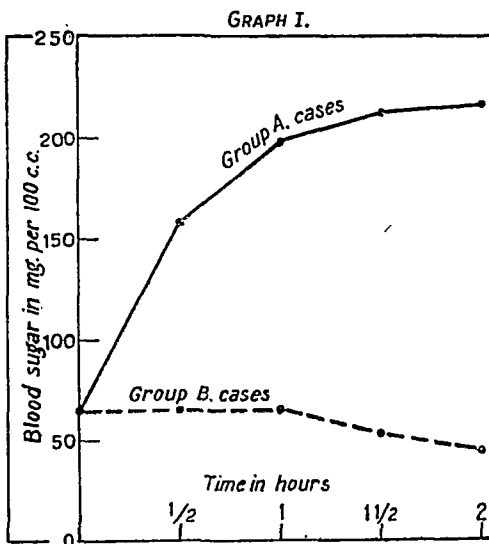
Effect of intravenous injection of glucose (0.2 gm. per kilo of the body weight) on the blood sugar in cases of group B

	BLOOD SUGAR IN MG. PER 100 C.C.					URINE SUGAR	
	Before giving glucose	15 minutes after glucose	30 minutes after glucose	45 minutes after glucose	1 hour after glucose	Before	After
Average results in the majority of cases.	70	325	246	200	195	nil	0.8%
Average results in rest of the cases.	65	190	134	85	60	nil	nil

These results are shown in graph II.

Œdema as has already been stated was an associated factor in the group B cases, the main reason being the marked decrease in the albumin content of the blood. This fact was

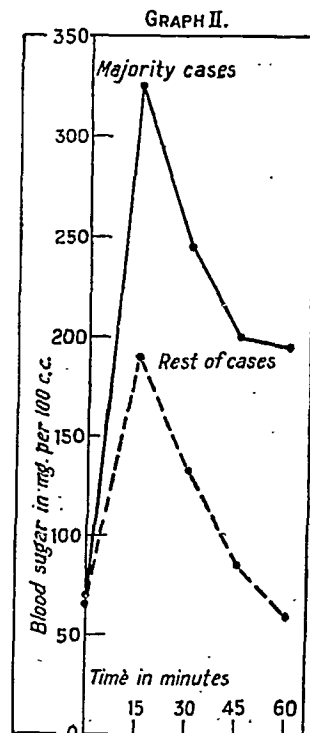
included cases suffering from inanition due to starvation. These patients were usually emaciated sometimes to an extreme degree, the subcutaneous fat often being completely absent.



also noted during the survey of the famine-afflicted areas in Europe during the last Great War. A low level of plasma protein due to lowering of the albumin content was observed in persons suffering from famine œdema as well as in malnutrition œdema.

Discussion

It appears clear from the results of the biochemical findings that the clinical classification made prior to it was justified. In group A are



The skin was dry, harsh and dehydrated, temperature subnormal and the systolic, diastolic and the pulse pressure reduced below normal, sometimes markedly. In group B on the other

hand are included cases of chronic malnutrition associated with intercurrent diseases. The outstanding clinical picture in these cases were inanition and oedema. It is curious to note that in many cases symptoms of the presence of diseases were often masked evidently due to extreme inanition. For instance malarial parasites were frequently found in the blood but with no splenic enlargement, the temperature being often subnormal. This was also true if the patient had other infections. It was also found that when the general condition of these cases improved they developed fever and other symptoms characteristic of the diseases they are suffering from.

Group A cases.—It appears from the observations made previously that the cases in this group were usually suffering from inanition due to effects of acute starvation, intercurrent diseases in these cases being often absent. It further appears that prior to real starvation there was not much evidence of malnutrition in these cases. It is thus evident that starvation for a period of 3 to 4 weeks could not cause any systemic damage except that the source of the reserve was being severely drawn upon but even then a sort of proper systemic balance was being maintained. The biochemical constituents of the blood, as shown in our results, were either normal or low. The urea and chloride excretion in these cases was also low evidently due to the fact that the intake was practically nil.

The only marked and noteworthy abnormality in cases of group A was a low tolerance for glucose, the blood-sugar curve after a test meal of glucose being markedly abnormal and often simulating diabetes. An explanation of this abnormal behaviour of the blood-sugar curve after a glucose meal has already been given. It appears that the sudden intake of a large quantity of glucose after a prolonged starvation caused a sudden rush of glucose in the blood stream which the sugar utilization mechanism could not cope with after such a period of complete disuse. It is interesting to note that subsequent sugar tolerance tests showed gradually better results till it became normal again. The degree of lowering in the glucose tolerance appeared to depend more or less on the actual period of starvation, *viz.*, the more prolonged the period of starvation was the greater was the lowering in glucose tolerance.

Group B cases.—Things were however quite different in the cases of this group. Here the majority of the cases were underfed and suffered from chronic malnutrition prior to their actual period of starvation. They had no 'reserve' to fall back upon hence they were, so to say, thrown off the 'balance'. It is noteworthy, however, that the patient gradually developed an unusual adaptability even though some of the chemical constituents of the blood became extremely low. For instance there was rarely any symptom of hypoglycæmic shock in these cases even though the blood sugar went down

to such an extreme extent as 0.04 per cent, the same may be said regarding serum protein which was reduced from 7.6 mg. per cent to an extremely low level of 3.7 mg. per cent. The absorptive mechanism of the alimentary tract was so seriously impaired with that even solution of glucose was not absorbed from the alimentary tract as shown by the peculiar 'straight' blood-sugar curve following the oral administration of 50 or even 100 gm. of glucose. The low total protein content of the blood, the marked fall in the albumin content of the serum and its leak through the kidneys, the abnormal rise in the globulin content, the reversal of the albumin/globulin ratio, etc., combined with the other abnormalities mentioned before brought about a condition in the patient which was extremely pathological, and unless prompt help was given the patient usually succumbed.

A Brief Outline of Treatment

General treatment.—It should be kept in mind that most of these cases are exposed to cold prior to coming to hospital and hence a good supply of clothing, blankets, etc., are necessary to keep the patient warm. Further, a large number of these patients are brought in a state of collapse which should be immediately attended to. The patient should be kept warm and warm fluids such as coffee with sugar, etc., should be given. In severe cases intravenous injection of a special preparation of protein hydrolysates containing vitamin B complex with glucose should be given. This consists of a mixture of 5 per cent glucose and 5 per cent protein hydrolysates which contain riboflavin, nicotinic acid and thiamin. It is of a clear port wine colour free from precipitate and turbidity. It is kept in screw-capped transfusion bottles, the quantity in each bottle being usually 200 c.c. which represents the average dose.

The body weight of these sick destitutes is reduced to an extreme degree and this fact should be kept in mind in selecting the dosage of drugs which should naturally be proportionately less. In usual practice half of the usual adult dose is administered. The patient should be kept in congenial surroundings as far as possible.

Dietetic treatment.—The general principles underlying the dietetic treatment in these cases should be as follows:—

1. An easily assimilable diet preferably in the fluid form including skimmed milk, *ghol*, glucose, fruit juice, etc.

2. It should have the maximum nutritional value with the minimum of bulk. Egg flip, shark liver oil, compound vitamin tablets and salts should be added to increase the nutritional and calorie value of the diet without increasing the bulk.

3. As the general condition of the patient improves further addition in the diet would be

necessary. This should consist of thin *conjee* made with milk, sooji and water and thin gruel prepared with dal, rice and vegetables, salts, condiments, etc.

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NOTE ON DIET SURVEYS CARRIED OUT IN THE CENTRAL PROVINCES AND BERAR

By D. M. ROY

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THE surveys were carried out during the latter half of 1945 in rural and urban areas. The findings are summarized as follows :—

(A) Rural

(i) Rice tract (Village Brahmapuri, District Chanda)

Diet surveys were carried out among 11 families of the poor agricultural labour class during the month of October 1945 over a period of 7 days. The intake of the various foods per consumption unit per day and the chemical composition of the average diet were found to be as follows (table I) :—

Comment.—The diet is adequate in calorie value but deficient in fat, calcium and vitamins A and C. The average monthly income per family in this group was estimated at Rs. 29-13-1 or per consumption unit Rs. 6-12-2 or daily income per consumption unit As. 2-7. The cost of a balanced diet per adult consumption unit in the rice tract at current controlled prices is calculated at As. 9-10½.

(ii) Wheat tract (Village Lugharbara, District Chhindwara)

Diet surveys were carried out in November 1945 among 14 families of the poor agricultural labour class over a period of 7 days. Findings were as shown in table II.

Comment.—The diet is adequate in calories but deficient in fat and vitamins A and C.

This diet contains a very high proportion of Teora (*Lathyrus sativus*) which provides the high protein and calcium content but is responsible for the causation of lathyrism, a considerable number of cases of which are reported in this district. The average monthly income per family in this group was Rs. 26-11-5 and the average monthly income per consumption unit worked out at Rs. 8-9-0 or As. 4-6 income per consumption unit per day. The cost of a balanced diet at current rates is calculated at As. 9-3¼.

TABLE I

Item	Ounces per consumption unit daily	Chemical composition	Quantity per consumption unit daily
Rice	21.5		
Wheat	Carbohydrate	669.7 gm.
Jowar	5.8	Protein	94.9 "
Pulses { Teora	1.7	Fat	23.0 "
Other pulses	2.8	Calcium	0.57 "
Leafy vegetables	0.14	Iron	26.8 mg.
Non-leafy vegetables	0.9	Vitamin A	777 I.U.
Fruit	Vitamin B ₁	444 "
Ghee and butter	Vitamin C	12 mg.
Vegetable oil	0.6		..
Milk and milk products	Calories	..
Meat, fish and eggs	0.55	Gross	3,306
Jaggery	0.02	Net	3,156

TABLE II

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	5.6	Carbohydrate	731.3 gm.
Wheat	16.5	Protein	198.0 "
Jowar	Fat	14.7 "
Pulses { Teora	15.4	Calcium	3.0 "
Other pulses	1.2	Iron	53.1 mg.
Leafy vegetables	0.5	Vitamin A	2,404 I.U.
Non-leafy vegetables	0.5	Vitamin B ₁	941 "
Fruit	0.03	Vitamin C	15 mg.
Ghee	0.01		..
Vegetable oil	0.06	Calories	..
Milk and milk products	0.4	Gross	3,904
Meat, fish and eggs	Net	3,754
Jaggery	0.2		..

(iii) Jowar tract (Village Kandli, District Amraoti)

Diet surveys were carried out in December 1945 among 10 families belonging to the poor agricultural labour class over a period of one week. The findings were as follows (table III):—

Comment.—The diet is adequate in calories but deficient in fat, calcium, iron, vitamin A and vitamin C. The number of students were 15 and the consumption units were 14.2.

(B) Urban

(i) Diet surveys were carried out among 4 school hostels at Nagpur during the month of

TABLE III

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	0.03	Carbohydrate	730.8 gm.
Wheat	0.17	Protein	121.2 "
Jowar	30.2	Fat	49.9 "
Pulses { Teora	Calcium	0.71 "
{ Other pulses	Iron	0.73 "
Leafy vegetables	2.34	Vitamin A	4.905 I.U.
Non-leafy vegetables	0.64	Vitamin B ₁	1.288 "
Fruit	Vitamin C	48 mg.
Ghee
Vegetable oil	0.85	Calories	..
Milk and milk products	0.65	Gross	3,832
Meat, fish and eggs	0.92	Net	3,682
Jaggery	1.2

Comment.—The diet is adequate in calorie value but deficient in fat and vitamin C.

The average monthly income per consumption unit in this group was Rs. 7-13-2 or daily income per consumption unit As. 4-2. The cost of a balanced diet in this tract at current rates is As. 9-9.

It is evident that in every rural tract the average income is seriously insufficient to meet the cost of an adequate (balanced) diet. On the other hand from the standpoint of pure calorie value the diets consumed are adequate to meet the needs of the people if these are calculated on an additional 150 calories per hour's work on a basis of 2,400 calories per day.

(iv) Students' Boarding House (Village Brahmapuri, District Chanda)

Diet survey was carried out in the students' Sree Chokha-mela Bidyarthi Boarding House during the month of October 1945 for a period of 7 days. The findings were as follows (table IV):—

August 1945 for a period of 10 days. The findings were as shown in table V (see p. 548).

Comment.—The diet was found to be adequate and balanced. The total number of students were 176 and the adult consumption units were 143.5.

(ii) A diet survey was carried out in the Hindu Orphanage (Sree Raj Kumari Bai Anathalay) at Jubbulpore during the month of November 1945 for a period of 4 days. The findings were as shown in table VI (see p. 548).

This diet is deficient in fat, calcium, iron, vitamins A and C and calories.

The number of orphans were 37 and the adult consumption units were 25.3. On clinical examination 22 orphans out of 37 were found with definite signs of one or more deficiency diseases.

(iii) A random diet survey was carried out during August 1945 among middle class lodging and boarding houses in Nagpur town. The findings were as shown in table VII (see p. 548).

TABLE IV

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	18.2	Carbohydrate	597.7 gm.
Wheat	5.6	Protein	89.2 "
Pulses { Teora	1.9	Fat	24.5 "
{ Other pulses	2.7	Calcium	0.57 "
Leafy vegetables	2.0	Iron	24.6 "
Non-leafy vegetables	4.7	Vitamin A	546 I.U.
Ghee and butter	Vitamin B ₁	533 "
Fruit	0.0	Vitamin C	47 mg.
Vegetable oil	0.6
Milk and milk products	0.6	Calories	..
Meat, fish and eggs	Gross	3,007
Sugar and jaggery	Net	2,857

TABLE V

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	6.7	Carbohydrate	472.1 gm.
Wheat	10.9	Protein	98.9 "
Pulses	1.8	Fat	80.2 "
Leafy vegetables	0.34	Calcium	0.86 "
Non-leafy vegetables	4.7	Iron	30 mg.
Ghee and butter	0.58	Vitamin A	3,848 I.U.
Fruit	2.4	Vitamin B ₁	758 "
Vegetable oil	0.9	Vitamin C	138 mg.
Milk and milk products	7.5	Calories	
Meat, fish and eggs	4.5	Gross	3,048
Sugar and jaggery	1.8	Net	2,808

TABLE VI

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	7.1	Carbohydrate	403.4 gm.
Wheat	9.6	Protein	64.6 "
Pulses	2.5	Fat	20.0 "
Leafy vegetables	Calcium	0.38 "
Non-leafy vegetables	3.8	Iron	23.7 mg.
Ghee and butter	Vitamin A	607 I.U.
Vegetable oil	0.38	Vitamin B ₁	654 "
Meat, fish and eggs	Vitamin C	38 mg.
Milk and milk products	2.2	Calories	
Fruit	Gross	2,067
Sugar and jaggery	0.15	Net	1,917

TABLE VII

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Rice	6.8	Carbohydrate	350.5 gm.
Wheat	5.2	Protein	62.2 "
Pulses	2.0	Fat	61.6 "
Leafy vegetables	Calcium	0.51 "
Non-leafy vegetables	7.0	Iron	18.6 mg.
Ghee and butter	Vitamin A	1,005 I.U.
Vegetable oil	1.4	Vitamin B ₁	568 "
Milk and milk products	4.0	Vitamin C	50 mg.
Fruit	Calories	
Meat, fish and eggs	1.9	Gross	2,187
Sugar and jaggery	1.7	Net	2,037

Comment.—This diet is deficient in protein, calcium, iron, vitamin A and calories.

The cost of a balanced diet for one adult consumption unit per day in the rice, wheat and jowar tracts of the province was worked out on the assumption that the actuals were purchased at the official controlled prices:—

	Tract	1940	1945
		Rs.	Rs.
Nagpur ..	Jowar	0-4-1	0-9-9½
Jubbulpore ..	Wheat	0-4-1	0-9-3½
Raipur ..	Rice	0-4-0	0-9-10½

Diet surveys were also carried out among 11 aboriginal families (Gonds) of the poor agricul-

tural class during the month of February 1946 over a period of 7 days in the Village Sitapar, P. O. Ghansore, District Chhindwara. The intake of the various foods per consumption unit per day and the chemical composition of the average diet are as given in table VIII (see p. 549).

Comment.—This diet is adequate in calories, taking 2,600 calories as the daily minimum requirement for an easy-going agricultural labourer. But it is deficient in fat, calcium, vitamin A and vitamin C.

The average monthly income per family in this group was estimated at Rs. 33-13-1 or per consumption unit Rs. 10-10-8 or daily income per consumption unit As. 8-8½. The cost of a balanced diet was estimated at As. 9-3½ which is therefore well beyond the means of the people.



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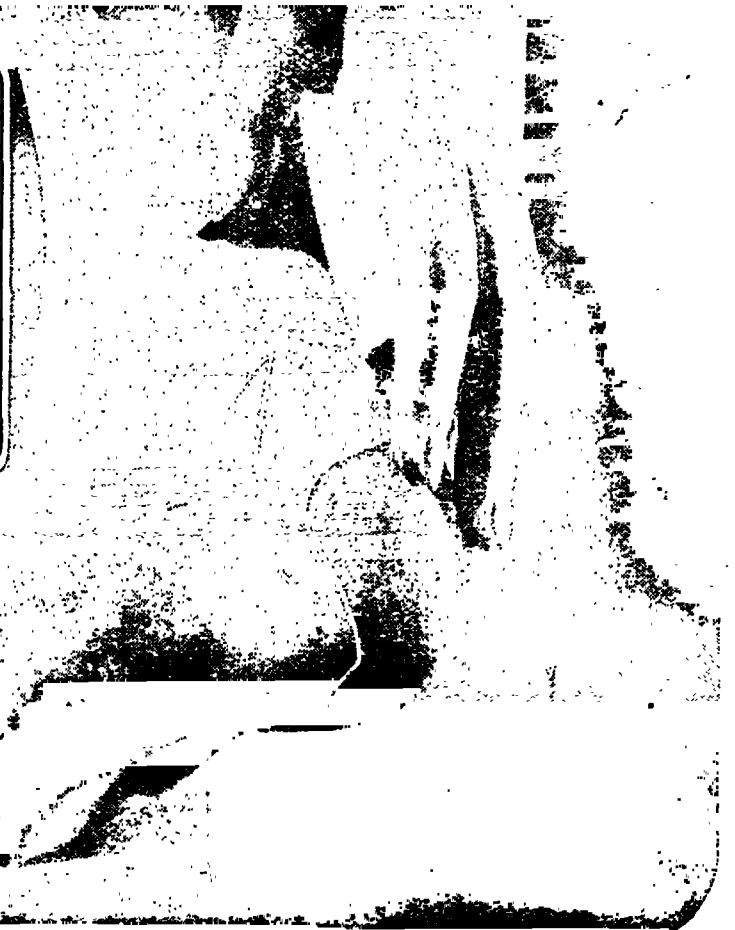
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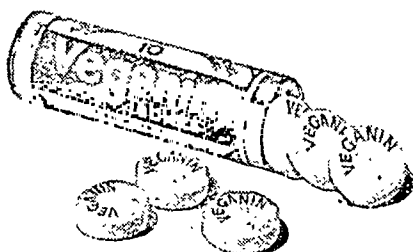


WOMEN AND THE CLIMACTERIC

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TABLE VIII

Item	Ounces per consumption unit daily	Chemical composition	Per consumption unit daily
Kudai	16.7	Carbohydrate	599.7 gm.
Kutki	3.9	Protein	112.5 "
Rice	1.5	Fat	20.5 "
Wheat	0.40	Calcium	0.67 "
Pulses	10.3	Iron	60.8 mg.
Leafy vegetables	0.54	Vitamin A	1,645 I.U.
Ghee and butter	0.01	Vitamin B ₁	1,102 "
Vegetable oil	0.13	Vitamin C	13.6 mg.
Meat, fish and eggs	0.83	Calories	..
Milk and milk products	0.23	Gross	3,023
Jaggery and sugar		Net	2,873
Non-leafy vegetables			

The method of cooking of the aborigines is rather interesting. The cereals consumed by the aborigines were millets, mainly kudai, kutki, sometimes kangni, sama, makia and less frequently rice and wheat. The millets are generally taken in the form of :—

(i) Pej—millet boiled in an excess of water and taken as a drink. This liquid preparation is specially liked by the aborigines.

(ii) Bhat or kalawa—millet boiled in a small quantity of water to a consistency of cooked rice.

(iii) Khichri—millet cooked with some dal.

(iv) Lapta—millet cooked in water to a thick liquid.

(v) Chapati—millet in the form of chapati is only occasionally taken by the aborigines.

The pulses are also consumed in the above form.

Though more surveys are desirable this can be taken as the general feature of the diet consumed by the aborigines. But the Baigas of Mandla differ in their dietary habits from the Gonds in the Chhindwara district who have migrated from the interior jungles and settled in places inhabited by Hindus. These Baigas eat the meat of animals such as rats, snakes, cows and any other animal they can kill and get. During certain periods of the year (September to January) when cereals are scarce the Baigas subsist mainly on wild tubers and roots. Attempts are being made to procure them here during the proper season and send them for chemical analysis.

My grateful thanks to Colonel L. K. Ledger, O.B.E., I.M.S., for his kind permission to publish this article.

Current Topics

Paralysis Agitans and Cervical Sympathectomy

By HAROLD DODD

(Abstracted from the *British Medical Journal*, i, 22nd June, 1946, p. 965)

HAROLD DODD reported the result of cervical sympathectomy on seven patients, three of post-encephalitic tremor and four of Parkinson's disease.

The procedure consisted in the removal of the stellate and first and second dorsal sympathetic ganglia on the opposite side to the limb most affected by the tremor. When both limbs were affected, then a bilateral cervical sympathectomy was performed at separate sessions on three occasions. The rationale of the operation is to increase the blood supply of the brain.

The results are as follows: There have been no deaths. Four patients are much better (two men and two women); three are unchanged. Those who are improved were aged 33, 35, 36, and 45; those who are unchanged were aged 38, 45, and 68. No patient is worse for the operation. In those improved the tremor is lessened and controlled by medicine, whereas formerly it was uncontrollable. In one woman the tremor was so violent that when she folded her arms during the consultation to try and steady them the body and chair on which she sat shook freely. Resumption of some work has been possible. One woman volunteered that she could write again; another that she could

sweep up and dust, previously impossible. The patients are brighter in personality and the mask face and eyes are improved; also the headaches. They still require medicine, but before operation, they were unhelped by it.

A. B. R. C.

The Clinical Value of Rectal Temperature Readings: A Comparison with the Oral Method

By H. W. HALES, M.D. (Cantab.)

(Abstracted from the *Medical Press and Circular*, 8th May, 1946, p. 310)

ORAL temperature readings are inaccurate indications of the true body temperature and are misleading in diagnosis and treatment.

Rectal readings show the true body temperature: the normal is 98.4°F. Any readings above this indicate fever.

A large series of rectal readings would prove that many diseases at present considered to be unattended by fever are really accompanied by a rise of temperature.

In cases where the elevation of the oral temperature is considerable a rectal readings might show a dangerous rise. This is of importance in heat stroke, malaria and treatment by very high temperature.

A. B. R. C.

Preliminary Report on the Evaluation of Penicillin in the Treatment of Yaws

By JAMES H. DWINDELLE

CHARLES R. REIN

THOMAS H. STERNBERG

and

ALBERT J. SHELDON

(Abstracted from the *American Journal of Tropical Medicine*, May 1946, p. 311)

PENICILLIN holds definite promise as a therapeutic agent in yaws. Its use in doses of 1,200,000 O.U. in adults and proportionate doses for children given over periods of four, two and one days respectively resulted in rapid clinical cures. The serologic response was not as striking as the clinical, but until more follow-up figures are obtained a full evaluation is not possible. The oil beeswax preparation of penicillin made it possible to treat patients on an ambulatory basis over one and two days with the same dose of penicillin given in aqueous solution to hospitalized patients over four days. The immediate clinical and serologic results obtained with penicillin in oil with beeswax appeared to be as good as those of the aqueous solution. The development of a successful one-day treatment schedule would be of great practical value in a country where large numbers of patients must be treated on an ambulatory basis in rural clinics.

R. N. C.

Syphilis and Parasyphilis [Three Observations on Indian Experience]

By S. D. S. GREVAL

(Abstracted from the *East African Medical Journal*, June 1946, p. 189)

1. FALSE positive Wassermann reactions, due to diseases other than syphilis, are common. They disappear with the disappearance of the disease.

2. Cases of parasyphilis are very rare indeed. This must be due to tellur influences, not to adequate treatment which is beyond the means of most people who contract syphilis. If that be so, the forecast for the post-war period in East Africa need not be gloomy.

3. The incidence of the disease amongst Indians has been overestimated in the past (20 to 22 per cent). It is really low (under 5 per cent) even in towns. In the country (where most of the population lives) it must be very low. The low incidence is dependent partly on socio-economic conditions (everybody of marriageable age is married and the main problem in life is food) and partly on the tellur influences (otherwise the population consisting mostly of poor people who cannot afford adequate treatment will not increase so rapidly as it has been known to do for some time now). Syphilis does not thrive in the tropics.

Malignant Malnutrition

(Abstracted from the *British Medical Journal*, 22nd June, 1946, p. 958)

In the tropics and in war-stricken European countries field workers have demonstrated repeatedly that the clinical picture shown by malnourished or starved populations may often differ widely from textbook descriptions. As Stannus has pointed out, unknown or ill-defined deficiency diseases probably far outnumber those whose characteristics are already plainly established. The condition of 'malignant malnutrition' recently studied in Uganda by Trowell and Muwazi presents problems which expose the limitations of existing knowledge. The first adequate description of this disease was given in 1933 by Cicely Williams, who

used to describe it by the native name of 'kwashiorkor', meaning a red boy or man. Although a reddish pallor of the skin and a softening and browning of the hair are frequently seen in affected native children, the change of colour in adults may be much less noticeable. Other features of the syndrome are loss of weight or failure to grow, oedema, an abnormal albumin-globulin ratio, crazy-pavement dermatosis, macrocytic anaemia, slight mental and neurological changes, and a deficiency bowel pattern, as indicated in the x-ray film. Although food passes through the intestines at a normal rate much undigested material is present in the faeces. The stools are loose, and in children there is steatorrhoea. The complete picture, however, is not always shown. The bowels may not be loose, and in children there may be no crazy-pavement dermatosis. In adults there is sometimes moderate osteoporosis. In specimens of liver taken by biopsy Gillman and Gillman in 1944 found fatty degeneration, which was sometimes preceded by pigment cirrhosis.

An examination of native diets indicated that very poor labourers subsist on inadequate amounts of food, which is deficient in most nutrients except vitamin C. To complicate the appraisal of the effects of malnutrition many of the natives suffered from malaria, hookworm disease, syphilis, and various protozoal infections. 'Malignant malnutrition' is often fatal, and the response to dietary treatment slow and uncertain. The presence of dermatitis might suggest that a form of pellagra is involved, but while treatment with nicotinic acid amide caused a peeling of the dermatosis a glazed and reticulated surface remained which showed no further improvement. Similarly, treatment with aneurin improved the appetite and increased the sense of well-being, but had no effect on the oedema. Liver concentrates and ferrous sulphate were beneficial to those suffering from macrocytic anaemia. Satisfactory cure of the syndrome as a whole, however, was effected only by the combined action of an improved basal diet and supplements of liver, milk, aneurin, and nicotinic acid.

Further research may reveal the lack of some single factor which is mainly responsible for 'malignant malnutrition'. In view of the high incidence of macrocytic anaemia, the recent work of Spies suggests that folic acid therapy is at least worth a trial. On the whole, however, it seems most probable that several deficiencies are involved, and that pathological changes are caused in the tissues which are not easily corrected even when the missing nutrients are restored. We are therefore faced with the possibility that a nutritional deficiency disease, with fairly well-defined lesions, may be due not to a single dietary defect but to multiple deficiencies.

Plague of Locusts in Italy

(Abstracted from the *Canadian Medical Association Journal*, Vol. 55, August 1946, p. 164)

CALLED the worst locust plague in Sardinian history, a devouring army of these insects, reported to be four layers thick, two and one-half miles wide and 30 miles long, was marching in the direction of the island's crop lands, leaving a barren waste behind it, according to a message from the UNRRA Rome office of May 7. 'Unless this menace is checked by July', said the dispatch, 'the plague of locusts may completely extinguish plant and vegetable life on the island, rendering existence there impossible for man and animals'.

The two main hatching centres of these pests, areas of 25,000 and 70,000 acres respectively, have sent forth myriads of insects that were still young and wingless, in a migration unprecedented in the island's history and in columns greater than any such invasions verified in Africa.

Sardinian authorities, lacking transport to meet the oncoming scourge, have been assisted by the delivery of all of UNRRA's motor vehicles in the island, intended for the anti-malaria campaign beginning in

September. As the intensity of the infestation was realized, the demand for poisoned bran as bait, was raised from 4,800 tons to nearly 20,000 tons and emergency shipments of sodium arsenite were sought from England. At the same time, UNRRA trailers and 135 four-wheel-drive trucks, being overhauled on the mainland, were pushed through reconditioning by double work shifts. Twenty of these already were sent to the island. Among other emergency measures, the Government is experimenting in locust-extermination by the use of 'cold smoke' fumes of hydrochloric acid and sulphuric acid sprayed by air pressure from drums carried by the trucks.

In the war against the record-breaking locust plague UNRRA has rushed quantities of the new pest-killer, gammexane, to the stricken island, together with additional transport vehicles to supplement those belonging to UNRRA and already in operation against the advancing hordes.

Five American transport planes on 18th May unloaded 10 tons of British-made gammexane in 60 drums to help combat the unprecedented plague in Sardinia. Simultaneously, ships at Oibia in the north and at Cagliari in the south, unloaded 30 more weapon-carriers, 10 jeeps and 30 trailers to speed the distribution of chemicals, personnel and equipment to the infestation points. Meanwhile, the struggle against the insects has been continuing, using such weapons as arsenite, flame-throwers, monochloride gas sprayed from UNRRA trucks, broom-beating and burning.

Gammexane, a relatively new compound, was flown over after a telegraphic search of Germany, Austria, Greece, Egypt, the Middle East and England revealed a lack of sodium arsenite available to mix with spoiled bran for poisoned bait. The compound has been used twice successfully in North Africa and is reported superior to arsenite in toxicity. It is harmless to animals and human beings.

By the end of May, after a seven weeks' battle, during which UNRRA experts employed every scientific means of locust extermination including techniques never used before, the invading hordes were halted, and except for some unforeseen development, victory was in sight, saving both the island's and the Italian mainland's precious crops.

Achromotrichia in Tropical Malnutrition

By WILLIAM HUGHES, M.D., M.R.C.P.

(Abstracted from the *British Medical Journal*, 20th July, 1946, p. 85)

THE circumstances in which achromotrichia or grizzling occurs might be classified as follows:—

1. In carnivora inhabiting the polar regions, where it occurs as a seasonal change. Genetic factors probably account for it here, although nutritional factors cannot be completely ruled out.

2. In middle and old age in man—*canities*. The process is common in negroes, although perhaps not so common as in white races. Sieve reported some improvement in cases treated with *p*-aminobenzoic acid, but his results have had no general confirmation.

3. Experimentally, grizzling and alopecia have been produced in various circumstances of malnutrition in animals, and particularly with deficiencies of the B₂ complex. Morgan and Simms produced grizzling in rats, which was cured by a filtrate containing pantothenate. This was confirmed by Unna *et al.*, using pantothenic acid.

Ansbacher identified *p*-aminobenzoic acid as an anti-grey-hair factor in rats. Inositol deficiency, according to Woolley, induces grizzling in mice. According to Martin and Ansbacher, inositol and *p*-aminobenzoic acid are complementary in the prevention of grizzling. Martin has reported grizzling in rats following a deficiency of 'folic acid'. The grizzling which arises from pantothenate deficiency in rats is associated with other signs such as blood-caked whiskers, 'rusty spots', and, post mortem, adrenal hemorrhages. Signs of panto-

thenate deficiency in the pig include an extensive dermatitis, ulcerative colitis, and spastic paralysis.

Kerlan and Herwick have reported negative results with calcium pantothenate, in a dosage of 20 mg. orally per day for six months, in the greying (*canities*) of middle and old age in man. The grizzling in our cases has been observed only in children and young adults, and responds to dietetic treatment. We are satisfied that the deficiencies concerned in both types of achromotrichia can be traced to factors of the B₂ complex. Our efforts at a more detailed analysis of the aetiology have led us to the following conclusions:

(a) The parakeratosis of recent acute kwashiorkor, by giving rise to rapid and extensive exfoliation, leaves a depigmented skin at the site of exfoliation. The normal dark curly hairs fall out and the new crop is sparse and depigmented. The missing factor is riboflavin.

(b) In primary nutritional achromotrichia there is a deficiency of some factor of the B₂ complex in the diet. This factor controls the colour and texture of the hair and may have some influence on haemopoiesis and the development of the teeth. The missing factor may be pantothenic acid.

(c) There is a large group of mixed cases in which both riboflavin and pantothenate deficiencies operate. It is possible that in many cases of kwashiorkor, riboflavin deficiency, by causing anorexia and inanition, would lead to a secondary deficiency of the B₂ factor concerned with pigment formation.

The Modern Treatment of Syphilis

By JAMES MARSHALL, M.D.

(Abstracted from the *Medical Press*, 31st July, 1946 p. 77)

No method of administration of penicillin has, so far, in my opinion, surpassed the results obtained in early syphilis by the use of arsenic and bismuth in properly planned standard or rapid schedules. My own observations suggest that a treatment combining penicillin with arsenicals gives better results than penicillin alone, and that the risks are slight if patients are carefully watched.

It is possible that further large-scale experiments with different plans of administration and higher dosage of penicillin may discover a treatment schedule which will give satisfactory results without concomitant treatment. Penicillin gives most spectacular immediate results, and at present I advocate that it should be used as a treatment of attack in all stages of syphilis, and that consolidating treatment with arsenicals, or bismuth, or both, should follow. I strongly advise against the use of any method of rapid arsenotherapy in general practice, as toxic effects can be alarming, and, without considerable experience, their advent cannot be forecast and offset.

The supplies of penicillin in oil are not yet regular, so that ambulant treatment of syphilis may not always be possible. If the aqueous solution has to be used the treatment can easily be administered in a nursing home or hospital (admission to the latter can be arranged with the director of the local venereal diseases clinic). In preparing aqueous solutions only a small bulk of sterile distilled water is necessary, and the individual dose can usually be dissolved in 2 c.c. A supply sufficient for 48 hours ahead can be made up and kept in a refrigerator until used.

Penicillin in oil-wax suspension is sometimes very thick, and the ampoule must be heated (*e.g.* by keeping in the trouser pocket, or putting it in the sterilizer for a minute or two) to make it sufficiently fluid to be withdrawn. A dry, warmed syringe and wide-bore needle facilitate extraction, and the bulk of each dose will vary according to the batch supplied.

The treatment schedules which I will detail have all been used by me, both in private and in clinic practice.

I repeat again my injunction that accurate diagnosis is essential for proper treatment, and urge that in

cases of doubt a specialist opinion should be sought both in questions of diagnosis and lines of treatment.

TREATMENT SCHEDULES

(1) *Early and latent syphilis*.—Penicillin 3,000,000 units. If the aqueous solution is used, give 60 intramuscular injections each of 50,000 units, 3-hourly, day and night, over 7½ days. If penicillin in oil-beeswax suspension is available, two injections each of 300,000 units are given daily (morning and evening) for 5 days.

Arsenic and bismuth. On the second and sixth days from the start of treatment 0.45 gm. neoarsphenamine is injected intravenously. Thereafter 0.6 gm. neoarsphenamine and 0.2 gm. bismostab (or some similar bismuth suspension in water) are administered once each week for 9 weeks. In the case of primary sero-negative syphilis treatment can then be suspended and observation begun.

In primary sero-positive, secondary, and latent syphilis I consider a further course of arsenic and bismuth advisable, and in such cases one injection of 0.2 gm. bismostab is given weekly from the eleventh to fourteenth weeks inclusive, after which a second 10-week course of injections of 0.6 gm. neoarsphenamine and 0.2 gm. bismostab is given before beginning observation.

If penicillin is not immediately available treatment should not be delayed on this account. The arsenic-bismuth schedule should be started and penicillin treatment interpolated as soon as possible.

(If an arsenoxide is used instead of neoarsphenamine, the arsenical injections must be given twice weekly throughout. The first dose should be 0.04 gm. mapharside or 0.06 gm. neohalarsine, and subsequent doses of 0.06 gm. mapharside or 0.09 gm. neohalarsine.)

Follow-up. In cases where treatment is apparently successful and serum tests are negative at the end of the treatment period, patients should subsequently be examined and have serum tests repeated every two months for the first six months, then every three months for a year, then every six months for another year. The final examination should include a serum test, examination of the cerebro-spinal fluid, and radiological examination of the heart and great vessels. In any case where treatment failure is suspected, the patient should be referred to a specialist in venereal diseases for assessment.

(2) *Late syphilis*.—Every case of late syphilis must be assessed individually, and it is impossible to lay down a schedule suitable for all.

Penicillin often causes rapid healing of cutaneous and osseocutaneous lesions, and varying degrees of improvement have been reported after its use in nearly all varieties of late syphilis.

At present I begin treatment with 4,000,000 units penicillin given in 100 doses of 40,000 units in aqueous solution every 3 hours, day and night, over 12½ days. (In cases where therapeutic shock is to be feared individual doses in the first 48 hours are reduced to 10,000 units and the treatment is lengthened accordingly.) Consolidatory treatment follows, and may consist of bismuth alone, or an arsenical (trivalent or pentavalent) and bismuth, according to the type of case, and should be continued for a minimum of 6 months, and often much longer. In cases of neurosyphilis (particularly of the parenchymatous type) progress must be followed by careful clinical examinations and by examination of the cerebro-spinal fluid repeated every three months in the first year, so that fever therapy may be instituted without delay if there is any evidence of treatment failure.

Follow-up. Life-long observation is necessary in all cases of late syphilis. At first the follow-up is on the lines indicated above for early syphilis, and later the visits can be reduced to once or twice a year.

(3) *Syphilis and pregnancy*.—Penicillin is reported to have good effects on mother and child during pregnancy. Miscarriage, stillbirth and neonatal death are averted, and children are born healthy in a high percentage of cases. My own few cases have all been treated on the

lines I have indicated above for early syphilis so far with excellent results.

(4) *Congenital syphilis*.—Good results in infantile congenital syphilis are reported with penicillin in doses of 40,000 units per kilo body-weight distributed over 7½ days. Infants and young children should always be hospitalized for specialized treatment.

Older children with the later manifestations of congenital syphilis should be treated on the lines laid down for late syphilis, and after the age of fifteen, full adult doses of bismuth and arsenicals can be employed. Results in these cases are rather equivocal, and in some conditions, such as interstitial keratitis, penicillin has not shown itself to be any better than other remedies.

Histamine and Allergy

(From the *Clinical Proceedings*, Vol. 5, April 1946, p. 81)

For many years, histamine has been thought to be responsible for many of the manifestations of allergy. There is no doubt that it plays a prominent rôle in this regard but it appears equally certain that other substances including peptones and possibly acetylcholine modify its action or entirely replace it as the effect or substance in hypersensitive states.

Although it has long been known that histamine is released from the tissues in response to various stimuli, nothing has been known of its chemical state before release and very little about its fate after release. Several papers have appeared recently which appear to throw light on these points, and the knowledge so gained is likely to be of great value in uncovering the pathogenesis of allergy and in providing new methods of treatment.

The finding that a number of proteolytic enzymes releases histamine from the tissues suggests that, in its inactive form, it is bound to other substances, probably amino-acids or proteins, by means of a peptide linkage. The observations of Edlbacher, Jucker and Baur that a number of amino-acids inhibited the action of histamine on isolated smooth muscle suggested to Ackermann that their imine= NH groups were competing with the like =NH group of histamine.

As the toxic action of histamine is dependent on its —NH^+ amine radical he suggested that the group anchoring the substance to its chemoreceptor in smooth muscle was the =NH imine radical. Rocha E. Silva carried this further and suggested that the histamine present in normal tissue was present in the inert form bound by its —NH^+ group to protein or amino acid. Disturbances of the protein by a number of means would release the histamine which would then attach itself to the smooth muscle by means of its imine radical.

He found support for this theory in a series of experiments in which he linked histamine to various substances by means of its NH^+ -group. The new compounds were inactive but the active histamine could be released by proteolytic enzymes. In another series of experiments he confirmed that arginine and a number of other amino-acids inhibited the action of histamine *in vivo* and *in vitro* and he synthesized a number of substances with free =NH radicals which were pharmacologically inactive but which similarly inhibited the action of histamine *in vitro* and *in vivo*. The inhibiting action of the amino-acids and these new substances were of an order that suggested that they were competing quantitatively with the imine group of histamine. Further, as would be expected on this theory, the substances he had produced by blocking the amine end of the histamine molecule also competed with histamine itself for the imine linkage.

While this work appears at first sight to be of only theoretical importance, it has possible practical applications to therapy. Histaminase has been disappointing in that its action has been irregular. This may be due to the fact that the histamine released in the cells is not readily accessible to it. In animal work, arginine has been given to counteract histamine but it has to be given in such large doses that it is very near toxic

concentrations that effects are produced. Its very high cost further makes it impracticable for clinical use. New substances produced along the lines suggested by Rocha E. Silva might be more active than arginine, non-toxic and cheaper.

Another interesting attack has been made on allergy on similar lines. Fell, Rodney and Marshall coupled histamine to proteins by its amine group. These histamino-proteins were then injected into animals resulting in antibody formation to the artificial protein. They showed that the histamine was the major hapten in the histamino-protein. Animals immunized in this way displayed a marked degree of resistance to anaphylaxis.

New American Antimalarial Compounds

(Abstracted from the *British Medical Journal*, ii, 24th August, 1946, p. 267)

THE first group includes chloroquin, or resoquin, also known as SN 7618, which is 7-chloro-4 (4-diethylamino-1-methylbutylamino) quinoline.

This compound has an interesting history. When the Allied Forces occupied Tunis in 1943 they found that a secret German preparation called sontoquin (later renamed 6911) had been sent there for trials against malaria. Workers at the I. G. Farbenindustrie had synthesized sontoquin before the war; but it was considered to be little better than mepacrine, and its further development was conducted half-heartedly. Supplies of sontoquin were taken to America and Britain, and the chemical formula was determined. Clinical trials in the U.S.A. of one of its derivatives—chloroquin—showed that it had important advantages over mepacrine. Large-scale trials confirmed this; mass production was begun, and if the war had continued another year, chloroquin would probably have displaced mepacrine as the main antimalarial in use among the American Forces. Its absorption, excretion, and distribution in the body resemble those of mepacrine, but it is colourless and does not stain the skin. It completely suppresses malignant tertian malarial infection, and adequate treatment of clinical attacks produces radical cure with complete elimination of the parasites from the body. All signs of benign tertian infection are suppressed so long as administration of the drug continues, but when this ceases relapse usually occurs. In order to suppress malaria in soldiers it is necessary to give 0.1 g. mepacrine every day. The same results may be obtained by giving a single dose of 0.25 g. chloroquin weekly, which is important as reducing the time-consuming supervision of drug administration to one-seventh of its previous level. In its general properties chloroquin challenges comparison with paludrine. One or other of these two compounds will almost certainly replace quinine and mepacrine; comparative tests in field trials are now taking place. Chloroquin has been tried on a much wider scale than has paludrine, but in many ways paludrine seems to be the more promising of the two.

Neither chloroquin nor paludrine can effect a radical cure of benign tertian malaria. All clinical symptoms disappear during administration of either drug, but on withdrawal, a relapse usually appears sooner or later. It is hoped that radical cures will be brought about by means of another new American compound—SN 13276. In 1943 there was much controversy over the merits of pamaquin (plasmoquin). Earlier work by Sinton in India has suggested that a combined course of pamaquin and quinine was more effective than any other remedy in sterilizing benign tertian infections. Owing to the absence of controls this work was open to other interpretations, and in addition pamaquin was unpopular, because it was apt to produce toxic reactions. The Malaria Committee of the Medical Research Council instituted comparative trials of pamaquin plus quinine and of mepacrine. These investigations were carried out by Kelleher and Thompson. They were statistically satisfactory, and the cases were followed up successfully. During the following six months about

30 per cent of the patients treated with mepacrine relapsed, as against 10 per cent of those treated with pamaquin and quinine. This proof of the value of pamaquin was communicated to the American workers, who instituted a very extensive study of the plasmoquin (8-aminoquinoline) series of compounds to find a more active but less toxic derivative. The most promising compound to emerge from this study is SN 13276.

Therapeutically it is as active as pamaquin in avian infections but is less than half as toxic to laboratory animals. In man a thrice-daily dose of 20 mg. SN 13276 is as well tolerated as 10 mg. pamaquin given in the same way. Volunteers in an American prison who were infected with the virulent South-West Pacific strain of *P. vivax* and treated with full doses of the new compound (plus quinine) appear to have been completely freed from the infection. Further trials are being undertaken in the U.S.A. and in Britain; until these are completed it is not possible to make a true assessment.

Black Tongue and Oral Penicillin

By P. D. BEDFORD

(Abstracted from the *British Medical Journal*, ii, 13th July, 1946, p. 63)

WITH the release of penicillin for sale by pharmacists on medical and dental prescriptions, its administration will become general. I venture to predict that one of its most common uses in general practice will be in the treatment of sepsis of mouth and throat by means of lozenges and sprays. I have personally observed melanoglossia in two instances as a concomitant of such treatment, and, having heard of a third from a colleague, infer that the condition will be seen with increasing frequency. This letter is written in order to apprise those who have not yet administered penicillin as oral lozenges or throat spray of a complication of treatment which, though innocuous in itself, may occasion alarm. It is hoped that bacteriological investigation of a sufficient number of these cases will elucidate the cause of this puzzling condition.

Case 1.—A previously healthy male, aged 28, reported with sore throat, hoarseness, and slight malaise of two days' duration. He was a moderate smoker (10 a day), not subject to sore throats. T. 99°F. (37.2°C.), P. 78; teeth and gums healthy; tongue clean; oro- and nasopharynx injected; tonsils moderately enlarged; R. tonsil oozing pus from several crypts; tender R. tonsillar lymphadenitis; no abnormality detected in other systems. Treatment: penicillin lozenges (gelatin base, 250 units per pastille), one to be inserted into the buccal sulcus and retained as long as possible; another to be inserted as soon as the first dissolved, and so on during the waking hours. The patient continued at work. He was advised not to smoke. No other treatment was given. *Second day* (after 12 lozenges): T. 98.2°F. (36.8°C.), P. 72; subjectively much improved; tongue clean; tonsils settling, pus not expressible from either; lymph glands not tender. *Third day* (after 9 more lozenges): Feels quite well; T. 97.8°F. (36.5°C.), P. 72; tongue lightly coated with yellowish fur; tonsils clean; R. tonsillar lymph gland palpable but not tender; oro- and naso-pharynx normal. Treatment discontinued; patient discharged cured. Total number of lozenges administered 21. *Fifth day*: Reported with 'black tongue'. The tongue was covered on its dorsal surface with a dark-brown fur. The edges and tip were clean and normal. The coat was thickest posterior to the circumvallate papillae and in the median sulcus anteriorly; it faded towards the tip and edges. The colour was most intense, indeed quite black, where the coat was thickest—i.e. in the median sulcus and on the posterior surface; these places looked like worn black velvet, the 'pile' being about 1/8 in. (3 mm.) in length. The edges of the coat were a dark brown, and the whole tongue had a moth-eaten, furry, velvety appearance. It was covered with a mushy brown detritus which left a dark-brown speckled stain on gauze; its removal did not materially affect the

appearance of the tongue. Apart from the tongue, there was no abnormality on examination. There was no malaise, no fetor, no unpleasant taste, and no dyspepsia. He admitted recommencing smoking yesterday. He denied the use of mouth washes or the ingestion of coloured confections; he had not sucked Brompton or other liquorice lozenges; he had, drunk strong tea, but this was his normal practice. He was reassured; no treatment was advised, and he was kept under observation. *6th to 10th days*: No appreciable change. *11th to 16th days*: Gradual thinning and disappearance of the fur from the lateral edges medially. The last area to clear was in the median furrow for about 2 cm. anterior and posterior to the circumvallate papillae. *18th day*: The tongue presented a perfectly normal appearance. He had remained symptom-free throughout. He had never suffered from the condition before. There was no family history of melanoglossia.

Case 2.—Male, aged 31; reported with sore throat and dry, irritating cough following a 'cold in the head, which always goes to my chest' three days previously. T. 98.2°F. (36.8°C.), P. 72; oro- and nasopharynx injected, dry, and glazed; tonsils absent (removed at age 23); tongue, teeth, and gums normal; other systems revealed no abnormality. Treatment: penicillin pastilles as for case 1 (gelatin base, 250 units per lozenge) and penicillin throat spray (250 units per ml.), inhaling deeply with each squeeze of the bulb, six squeezes half-hourly during the waking hours. No other treatment was given. He was advised not to smoke. All symptoms and signs had subsided after two days and treatment was discontinued (number of penicillin lozenges 19). Two days later (*i.e.* four days after commencing penicillin therapy) he reported with a heavily coated dark-brown tongue which, by the next day, was similar in every respect to that in case 1. He had not smoked, gargled, nor used a mouth wash. He had sucked no coloured confection. He presented no sign of syphilis or other disease. There was no fetor, dyspepsia, or unpleasant taste, but he had suffered some embarrassment from facetious comments from his acquaintances. The condition remained *in statu quo ante* for five days and then rapidly regressed. Sixteen days after his first reporting, his tongue had regained normality.

The two cases described above were, I have very little doubt, of the 'mycotic pseudo' variety, and, although they may have arisen fortuitously, the rôle played by penicillin is strongly suggestive of a cause-and-effect relationship. A likely aetiological view is that the fungal spores (and chromogenetic bacteria) are not uncommonly present in the air and mouth, but their growth is inhibited by the products of the normal buccal symbiotic flora. When penicillin alters this biological balance (*cf.* sulphaguanidine and streptomycin in the bowel) conditions then become less inimical to the growth of the organisms of 'black tongue', which clinical condition may then arise. Such a theory would explain the 'mycotic' cases unconnected with penicillin, the normal biological balance being disturbed by certain local irritants and antiseptics.

Stilbœstrol

(From the *British Medical Journal*, ii, 28th September, 1946, p. 468)

A CROWDED audience at the international meeting of the British-Swiss Medical Conference at Basle listened to an exposition by Prof. E. C. Dodds on oestrogens in cancer. He referred chiefly to the treatment of prostatic cancer by stilbœstrol. The result of the introduction of oestrogens, he said, had been a widespread tendency to 'dose' with stilbœstrol everybody who had any type of cancer, but a careful examination of the claims showed in almost every case an absence of justification for the widespread use of this and its sister substances in the treatment of carcinoma in general. The interesting fact did appear, however, that in inoperable carcinoma of the breast some 5 per cent of cases received a definite benefit, varying from

a slight improvement in the local condition to a tendency of a fungating carcinoma to heal, and in a few cases to the disappearance of the lesion. But in the treatment of carcinoma of the prostate the results were clear-cut. The opinion of expert urologists of most countries was that such patients should be treated with stilbœstrol, though even here it was in no sense a cure; it was a control, a means of palliation, lasting for varying lengths of time, in some cases for the whole five years over which the observation had extended, and sometimes only for six months.

In some later discussion on Prof. Dodds' communication Dr. J. McMichael pointed out that the patient with cancer of the prostate very frequently had no very definite prostatic symptoms. He might arrive at hospital with symptoms due to secondary deposits, and an examination of the prostate by means of x-rays might show calculi, which possibly co-existed with carcinoma. A diagnostic measure which had been suggested was the administration of testosterone, 50 mg. daily, upon which the acid phosphatase level, if it had not already risen, would steadily rise. In one patient the answer was clear: there was a steady rise of acid phosphatase level, which fell as soon as administration ceased, and this patient, after being given stilbœstrol, was able to leave hospital. But in another case the response to testosterone injection was very irregular, falling while injections were continued, and rising to a peak after they were stopped. This patient also was put on stilbœstrol, but went downhill quickly and died with massive secondaries about four months later. Sir Heneage Ogilvie said that he had the impression that the Americans were now preferring castration to stilbœstrol.

A Case of von Recklinghausen's Disease with Marked Thickening of Nerves

By N. MUKERJEE

(Abstracted from the *Leprosy in India*, Vol. 18, April 1946, p. 71)

1. MARKED thickening of multiple nerves in a person not suffering from leprosy has been discussed.
2. The thickening was not associated with any motor or sensory changes.
3. von Recklinghausen's disease was responsible for the condition.

Study of Leprosy in a Family

By DHARMENDRA

and

N. R. SEN

(Abstracted from the *Leprosy in India*, Vol. 18, April 1946, p. 54)

SEVEN cases of leprosy have been found in a family of 28 members.

In all the patients the disease has been mild, in none it is of the more serious (lepromatous) type.

No source of infection can be ascertained with certainty. It appears that the disease was acquired from some neighbours in Rangoon who were suffering from leprosy, probably of the lepromatous type.

The fact that as many as seven members in the family acquired the disease through contact with neighbours, would indicate that the contact was close and frequent. However, the fact that in spite of the close and frequent contact none of them developed the disease in the serious form, would indicate a comparatively high resistance of the family to leprosy infection.

The presence of comparatively high resistance of the family to leprosy infection is supported by the results of the lepromin test. With one exception all the members were lepromin-positive.

The single finding of a negative lepromin reaction was made in a person who was probably exposed to infection along with the other members of the family, but who did not develop the disease. This is considered to be an anomalous finding.

The Serologic Diagnosis of Endemic Typhus III. The Incidence and Titre of Complement-fixing Antibodies in Random Samples of the Population in Endemic and Non-endemic Typhus Areas

By MARY B. JOHNSON, B.S.

and

SAMUEL R. DAMON, Ph.D.

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 31, No. 5, May 1946, p. 550)

In a section of the United States, where typhus is endemic, an examination of sera for complement-fixing antibodies from a random sample of the population shows the incidence of reactors to be high.

In a non-endemic area, the incidence of reactors is almost nil.

The titre of complement-fixing antibodies detected in presumably normal individuals varied from 1 : 4 to 1 : 256.

The significance to be attached to a positive complement-fixation test for typhus in a febrile patient living in an area of endemic typhus must be weighed by the foregoing observations.

The Reactions of the Uterine Blood Vessels before, during and after Pregnancy in Elephantulus

By C. J. VAN DER HORST

and

J. GILLMAN

(Abstracted from the *South African Journal of Medical Sciences*, Vol. 11, April 1946, p. 103)

By virtue of the characteristic modifications which occur in the uterine artery of *Elephantulus* it is possible histologically to discriminate at a glance between the uterus of a parous and that of a virgin animal. The distinction is based on a marked sclerosis of the tunica externa of the artery. Brambell and his school have used this modification of the uterine artery as an obvious indication of the age of the animals in their collections. This sclerosis is produced by an increase in the number and the density of the collagen fibres as well as of the elastic fibres. The increase in the elastic fibres suggests that new elastic tissue can be formed in the wall of an involuting artery.

The sclerotic uterine artery of the parous animal is capable not only of undergoing softening but also of making all those adjustments in structure which are seen in the uterine artery of a primiparous animal.

Once the decidual reaction has become well marked the uterine artery becomes greatly dilated. Since the muscle cells only form a single and discontinuous layer underneath the endothelium they do not appear to be able to regulate the bloodflow through the same extent as can the muscular uterine artery of the non-pregnant animal. The dilated artery appears to have only a passive rôle in transmitting arterial blood to the placenta. The mechanism for regulating this circulation most probably resides in the uterus.

One feature of particular interest is the restriction of the decidual reaction to the arterial wall; the wall of the vein throughout the whole of pregnancy preserves its original structure. This difference makes it easily possible to distinguish the artery from the vein both in the wall of the uterus and in the mesometrium.

After parturition the arterial wall undergoes rapid involution; the decidual cells disappear and their place is taken by an abundance of elastic and collagen fibres.

During this involution the original dilated lumen of the artery is reduced to a narrow cleft lined by a thin lamina of smooth muscle.

Benninghof, in reviewing the relevant literature on the involution of the uterine artery in the human female after parturition, supports the view that a new lumen is established at this time. From our observations we are reasonably satisfied that the involution of this artery occurs in a manner similar to that described for *Elephantulus*.

The fact that a sclerotic artery is capable of undergoing softening and of making the requisite adjustments, indistinguishable from a non-sclerotic vessel, would seem to indicate that arteriosclerosis is not necessarily an irreversible phenomenon. In the case of the uterine artery such reversibility is most probably determined by endocrine activity. Provided the appropriate stimulus is applied, there is no reason why the artery in arteriosclerosis should not renew itself in the same manner occurring as a natural phenomenon in the uterine artery of *Elephantulus*.

Spontaneous Rupture of the Spleen during a Malarial Rigor

By K. R. TORODE

(Abstracted from the *Medical Journal of Australia*, Vol. II, 21st September, 1946, p. 414)

CLINICAL RECORD

THE patient was brought to hospital by ambulance at night and admitted with the provisional diagnosis of malaria. He had been discharged from the army three months previously, and had a history of severe dysentery while in the tropics, but had never had an attack of malaria, and six weeks previously he had ceased taking his suppressive dose of 'atebrin'. He had been in good health till the day of his admission to hospital, when he had become nauseated and faint, and begun to shiver and had been slightly delirious and had had several loose bowel actions.

On examination, the patient was a well-developed male, aged 22 years. He was slightly pale. His temperature was 101°F., his pulse rate was 120 per minute and no abnormality was detected in his heart or lungs. Slight epigastric and left hypochondriac tenderness was present; the spleen was thought to be palpable.

In accordance with the usual routine treatment in an unproven case of malaria, and indeed in view of the largely negative history, the patient was placed under observation. On the following day and the succeeding morning he was symptom-free, his temperature and pulse rate were not elevated, and he had walked to the bath room. About midday he felt nauseated and began to have a mild rigor. A blood smear was examined, with positive result, and 10 grains of quinine were administered orally at 2 p.m. At about 2-30 p.m. he became increasingly pale and uneasy and his pulse rate was 120 per minute; the foot of the bed was raised. By 3 p.m. the patient appeared to be entering a state of profound shock, and the intravenous administration of serum was commenced and a small intravenous dose of quinine was given. At this stage he complained of severe pain in the back over the renal angles; the abdomen was lax, and splenic tenderness was present. Blood donors were called and as soon as possible blood transfusion was substituted for the administration of serum. In the interval the patient had completely collapsed, and by 4 p.m., he was comatose and almost pulseless. A second amount of 600 millimetres of blood was taken from the donors and rapid transfusion was continued; but the patient was completely pulseless and moribund in spite of repeated injections of 'coramine' and adrenaline; at no time did improvement occur. Serum was again substituted while a further donor was called and blood was taken; but by the time this was accomplished it was too late, and the lad died at 8-30 p.m.

In the belief that this patient must have died from a rupture of the spleen superimposed on a severe

malarial attack, necessary permission was obtained and a post-mortem examination was carried out. The heart, lungs, alimentary tract and kidneys appeared normal, and the liver was normal also except in appearing slightly larger than average. The peritoneal cavity contained pints of blood clot and serum, obviously originating from the enormously enlarged spleen. The spleen measured approximately 12 by 6 by 4 inches, and weighed about 4 pounds; in its postero-inferior surface was a rupture covering an area of about 6 square inches.

Reviews

PRINCIPLES AND PRACTICE OF WAR SURGERY : WITH SPECIAL REFERENCE TO THE BIOLOGICAL METHOD OF TREATMENT OF WOUNDS AND FRACTURES.—By J. Trueta, M.D.Hon., D.Sc. (Oxon.). Third Edition. 1946. William Helne-mann (Medical Books) Limited, London. Pp. xvii plus 426. Illustrated. Price, 42s.

THIS book now deservedly in its third edition needs no further recommendation than that. It entered the ranks of the classics on Traumatic Surgery long ago.

The new section on developments since D-day is important. New Penicillin and Sulpha techniques are described and their correct place in the management of cases of Major Trauma indicated.

This edition places more weight than ever on first principles and it is a joy to see especially the attention given to the point, so often forgotten in this age of 'Wonder drugs', that there can be no effective substitute for correct surgery.

Many critics are answered and wise use made of the suggestions of others.

A good book not to be set aside in these troubled times of Peace nearly on account of the inclusion of the word *War* in the title. 'The Principles of the Management of Major Trauma' would be a better title perhaps—or at least a suitable sub-title.

A. T. A.

ANATOMICAL ATLAS OF ORTHOPÆDIC OPERATIONS.—By L. S. Michaelis, M.D. 1946. William Helne-mann (Medical Books) Limited, London. Pp. 67, with 73 illustrations in colour. Price, 25s.

THIS small but costly book is unfortunately neither anatomical nor Atlas-like.

The diagrams are distinctly poor in comparison with the average production. They do not ease the amount of work to be done by the reader, as he might expect from a work calling itself an Atlas, because their very sketchy nature requires a considerable effort to visualize one's whereabouts.

Why the Surgery of approach to long bones and joints should be called orthopædic is not easy to imagine. These approaches were in use long before orthopædics became a special branch; they are still used by the general surgeon. Many of the approaches illustrated have now been superseded by more extensile ones.

The idea behind the book is very good, but the final product falls short of the mark. An Atlas of Operations in these days is an ambitious undertaking.

A. T. A.

THE DIABETIC ABC: A PRACTICAL BOOK FOR PATIENTS AND NURSES.—By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Ninth Edition. Published by H. K. Lewis and Co., Ltd., London. Pp. vii plus 79. Price, 4s.

LITTLE comment is necessary on the ninth edition of Dr. Lawrence's book. The very fact that the book has been published 18 times (including 9 reprints) within a period of about 18 years amply proves the popularity of the work.

This short practical book is written mainly for the diabetic patients who use the author's diet scheme, particularly the Line Ration Diet, which he introduced in 1925. By means of this simple yet varied fixed diet scheme the patient, under instruction of his doctor, is able to choose his diet according to his taste without elaborate calculation of food and caloric values of the various foodstuffs. This form of dietetic treatment, however, has not found much favour with the patients in this country, the chief reason being that the nature of the foodstuffs varies so widely in the different parts of the country (according to race, religion, etc.) that a fixed diet scale of this form appears to be unsuitable for general use.

J. P. B.

FOOD AND NUTRITION: THE PHYSIOLOGICAL BASES OF HUMAN NUTRITION.—By E. W. H. Crulckshank, M.D. (Aberd.), D.Sc. (Lond.), Ph.D. (Cantab.), M.R.C.P. 1946. E. and S. Livingstone Limited, Edinburgh. Pp. vii plus 326. Illustrated. Price, 16s.; postage 7d. (home)

IN the first few chapters the author deals with the problem of world malnutrition and in particular the problem of nutrition in Great Britain. After briefly referring to the chief contributory factors of malnutrition of which unequal distribution of food is one, he rightly says that it is the eastern and tropical countries which suffer most from grossly deficient diets as judged by scientific standards. He gives a brief outline of the state of nutrition in some of these countries including India where a large proportion of the people never approach physiological requirements with respect to dietaries. The fact that certain Indian races are better off in this respect than others is due in no small measure to their diets containing such articles as freshly ground whole wheat (atta), ghee, milk, etc. We heartily agree when he says, 'Probably the most important advances which could take place in India would be to increase dairy farming and place agriculture on a sound scientific basis'. In contrast is the picture of Great Britain in which he gives an account of the advances as result of scientific advice, and he shows how that country managed to efficiently feed the nation during six years of the war although the supplies of meat, eggs, bacon, sugar, etc., were all greatly reduced.

Coming to the subject-matter of the book, the author has given a clear and concise account of food and nutrition, dietary planning and social and economic aspects of food. His views are sound, though at times dogmatic. Surely it is an exaggeration to say that in the Orient vitamin-B₁ deficiency plays an important part in high infantile mortality and morbidity. His implication that the same vitamin deficiency seriously affects the reproductive capacity of women is not borne out by facts. There are chapters on milk, bread and protein-rich foods, and there is also a chapter on vegetarianism in which he gives some very sensible advice on diets. The book contains much practical information and can be recommended. Both its size and price are reasonable.

R. N. C.

SIR W. ARBUTHNOT LANE, Bart., C.B., M.S., F.R.C.S., HIS LIFE AND WORK.—By W. E. Tanner, M.S., F.R.C.S. Baillière, Tindall and Cox, London. Pp. 192, with 1 portrait. Price, 15s.

A VERY powerful figure of the past requires a master pen to bring to life the man that was so that those who did not know him may enjoy his company as much as those who worked with him. Mr. Tanner's book, whilst covering the main events of the life of Arbuthnot Lane, cannot be said to accomplish this ideal. I doubt whether the author would claim that it did. It appears that he has written a short sketch of the life of his revered master and friend in humble commemoration.

The position of the opening chapter on 'Lane as I knew Him' is of great interest. Should a biographer with intimate personal knowledge of his subject open

with a chapter such as this? Should not the whole book contain 'Lane as I knew Him', that is the author's interpolation of the Man, peeping out through each related event? In this short book this chapter would have been better placed in the heart of the story where it chronologically belongs.

In places the style is awkward and a constant repetition of 'In 1895 Lane published.....; In 1896 he gave an account.....; In 1898 he was advocating.....', etc., as short paragraphs, one after another, is monotonous and is the result of an effort to put too much factual information into a small space.

However, the main story is interesting and for those who did not know Lane and his work it is well worth reading. There are many enlightening points about his work and teaching which correct present misrepresentations.

A. T. A.

'CHILD AND ADOLESCENT LIFE IN HEALTH AND DISEASE': A STUDY IN SOCIAL PÆDIATRICS.

—By W. S. Craig, B.Sc. (Glas.), M.D. (Edin.), F.R.C.P.E., F.R.S.E. First Edition. 1946. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xvi plus 667. Illustrated. Price, 25s. (with complete index); postage, 7d. (home)

THE author says that the number of specialists in the various fields reflects the many perplexing problems to which infants and children may give rise and sounds a note of caution for the future. He thinks that the present-day picture of the provisions for the care of child life and health can be compared to an unfinished jig-saw puzzle. The aim of this book is to describe the puzzle in its present unfinished form, and as an aid to solving the puzzle, explain how the past progress has been achieved. Thus, in the first seven chapters, he describes in detail how and what were the attempts made to solve the problem in the past, how the movement first started by private philanthropy and

voluntary effort, gradually gave rise to voluntary hospitals and beginnings of pædiatrics, Poor Law, care of the destitute child, welfare of school-children, infant and child welfare, recognition of some special needs of children and adolescents. In the next eight chapters, the author describes the care that is being taken of the child life and health at the present day. Under this he describes in detail homelessness, the juvenile in need of care and protection, the maintenance of health, help for the handicapped, treatment of sick children, etc. The lessons we can get from the past and present history, and the principles which should guide us to develop future standard methods for care of child and adolescent life are dealt with in the next chapter. The next few chapters deal with important legislations concerning this.

The author is quite justified in saying that whether as a member of a family or of the community, as a person interested in local or national government, or as a subscriber to charity organizations, the citizen should have opportunities of acquiring a knowledge of the needs of the child and adolescent, and this book serves the purpose in a most efficient way.

A. B.

BOOKS RECEIVED

1. Feeding the Worker. Canteens in Industry, No. 9, September 1946. Published by the Government of India, Department of Food, Department of Labour, New Delhi.

2. Nutrition. Bulletin No. 22, October 1946. Published by the Department of Food, Government of India, New Delhi.

3. The Ross Institute of Tropical Hygiene, India Branch, Report of the Committee of Control for the year ended 31st July, 1946. Published by the Office of the Committee of Control, Royal Exchange, Calcutta.

Correspondence

STORAGE OF PENICILLIN

SIR,—May I draw the attention of the medical profession through your esteemed columns, to the way in which penicillin is transported and stored in various cities. It is sent from big centres of distribution like Delhi, Lahore, etc., by post or rail in wooden packages, taking in ordinary course four to six days to reach its destination.

The medical stores in different cities are not at all particular about keeping penicillin vials in either refrigerators or ice-boxes. I have seen them lying in almira's like ordinary medicines.

Due to this negligence, potency of penicillin is either considerably diminished or completely destroyed.

Will the Indian Medical Association or the Indian Medical Council take up this question and recommend to the Government to compel the stores to keep penicillin under suitable temperature or in default to cancel their licences?

Yours, etc.,
RAJENDRA SINGH.

MEERUT CANTONMENT.

VACCINATION FOR SMALLPOX

SIR,—In your September issue under the correspondence column a case of unsuccessful vaccination has been recorded. In my experience there is a similar case. The person was vaccinated for the first time when about eight months old without any success; was revaccinated a month later without any reaction. Since then within the last twenty years she must have

been revaccinated at least ten times, results were always unsuccessful. The question of unreliability of vaccine lymph used does not arise as some cases vaccinated in the same batch were successful.

The mother of the case in question had an attack of smallpox in her own childhood. Could it be an instance of hereditary immunization? The brother and sisters of the case quoted behaved normally.

Yours, etc.,
OM PRAKASH, M.B., B.S.

RANGOON.

SIR,—In continuation of my letter published in your September 1946 number (p. 390), this child was vaccinated again at the age of nine months with complete success.

(Sd.) Illegible,
LIEUTENANT-COLONEL, I.M.S.,
Superintendent,
King Edward Memorial Hospital,
Secunderabad-Deccan.

(This correspondence refers to the vaccination of an infant who did not 'take'.—EDITOR, I.M.G.)

VITAMINIZED CHOCOLATES

SIR,—This morning's post brought a circular letter from a firm of manufacturers describing their vitaminized chocolates. The letter says, 'Each chocolate

weighs 15 gr. By taking 3 chocolates—an adult daily dose—you have as if taken :—

More vitamin A than in 2 lb. of fresh milk.

More protein than in 1 lb. of fish.

More naicin (? niacin) than in 6 slices of enriched bread.

More vitamin D than in 10 ounces of butter.

More vitamin B than in $\frac{1}{4}$ lb. of peas.

More vitamin G than in 1 lb. of meat.

More vitamin C than in 4 ounces of orange juice.

More food energy than in 2 cups of ice cream.

More calcium than in 6 eggs.

Many of these statements are grossly wrong and misleading. According to Health Bulletin No. 23, the lowest protein content of fish is 20 per cent (19.9 to be exact). One pound of fish therefore contains more than three ounces of protein. Assuming that the whole of this wonderful chocolate consists of protein, 3 such can yield only 45 grains (about 3 gm.) of protein!

The vitamin B (by which, I suppose, is meant B₁) content is claimed to be more than in $\frac{1}{4}$ lb. of peas. According to the Health Bulletin again, 100 gm. of peas yield 150 international units of B₁ when dry, and 120 when green. Even taking the lower figure, $\frac{1}{4}$ lb. of peas (which is more than 100 gm.) yield at least 120 units whereas 3 chocolates yield (as mentioned in the same letter) only 50 units!

Coming to vitamin C, 3 chocolates (which contain 100 units, i.e. 5 mg. only, again according to the same letter) are said to yield more vitamin than 4 ounces of orange juice! This quantity of orange juice should yield at least 60 mg. or 1,200 i.u. of vitamin C!

As to calories (called food energy), the statement is only a howler. Assuming that ice cream contains nothing but cow's milk and a cup is so small as to hold only an ounce, two cups should yield 36 calories! And we are told that three bits of this stuff weighing only 3 gm. give 'more food energy' than 2 cups of ice cream! Even if the tablets are all fat (which they are not; remember the protein farce) they can yield only 27 calories.

Even at the risk of being dragged into the law-court, people who make such preposterous claims should, I believe, be exposed.

Yours faithfully,
K. A. SHAH.

AHMEDABAD,
12th November, 1946.

[Dr. K. A. Shah has raised an important question in regard to indiscriminate advertisements by commercial firms on their medicinal preparations. The word 'vitamin' has somehow caught hold of the imagination of the general public and this is not confined to the people of India alone. Skilful advertisements have been very successful and India has become the dumping ground for medicinal preparations manufactured in other countries and where Drug Control Acts prohibit their sale in the countries of their origin. Several articles have been published within recent years in the *I.M.G.* on this aspect, and pleas have been put forward for strengthening measures to prevent such a state of affairs.

Food value calculations made according to the advertisement, taken as a whole, do not confirm the boosting and at least the figures for 'protein content' and 'food energy (calorific value)' contain preposterous claims. The rest of the items we will give the 'benefit of doubt' in the absence of any contrary statement and take it for granted that the chocolates are fortified with vitamins and calcium. We do not condone this and say that it is a happy state of affairs. If the product is fortified, the amounts of the substances added should be clearly indicated in order that the consumer gets his money's worth.

The example of this firm once again emphasizes the need for strict drug control and an authoritative laboratory to examine the claims and certify them before which such products should be prohibited for sale to the general public.—K. R.]

Any Questions

ATTA POISONING

SIR,—I have read with great interest your paper on 'Poisonous foodgrain: wheat mixed with *Lolium temulentum*' published in the August issue of the *Indian Medical Gazette*.

I have recently come across a case of poisoning of a similar type as described in your paper. Several villagers of 7 or 8 villages had gone out of sense and suffered from vomiting and shivering. Their trouble might be due to eating a particular supply of atta. I have not been able to detect any poison in the atta, but have a feeling that the poisonous character might be due to the presence of crushed seeds of *L. temulentum* in it. I shall be obliged if you will kindly let me know how to substantiate this possibility.

Yours, etc.,
N. GHATAK,
Chemical Examiner to Government,
U. P., Agra.

[The stock of grain from which the atta was made may be traced and searched for lolium seeds.

From the atta itself the starch grain may be compared with the starch grain from known lolium seeds, under the microscope. As pointed out in the paper, there will be 'a sharp microscopical difference between the wheat and lolium starch grains present in the endosperm of each seed'.—EDITOR, *I.M.G.*]

MEPACRINE IN MIXTURES

SIR,—Mepacrine hydrochloride being soluble in water may be served in a solution from the out-patient department, its colour being masked by tincture cardamom co. particularly in patients who have an antipathy for the yellow tablets. Can it be combined in mixtures with alkalis and spirits as in cases of malaria with bronchitis or with acids such as in tonic mixtures in convalescent patients?

Yours, etc.,
J. C. BHATTACHARJEE, I.M.P.,
Assistant Medical Officer,
D. H. Railway.

THAKURGANJ,
1st December, 1946.

[Being a hydrochloride salt it is not compatible with alkalis. Besides, a tonic mixture, as a rule, is continued for some time. As mepacrine cannot be so continued it is best to give it as an antimalarial remedy only.—J. C. G.]

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL L. K. LEDGER, O.B.E., I.M.S., assumed charge of the Director of Public Health, C. P. and Berar, in addition, from 1st November, 1946.

Lieutenant-Colonel W. T. Taylor is appointed as Additional Deputy Director-General, Indian Medical Service (Stores), with effect from the afternoon of the 4th October, 1946.

Lieutenant-Colonel H. S. Ahluwalia, I.M.S./I.A.M.C., is appointed to be Medical Officer, Civil Station, Barrackpore, with effect from the 1st August, 1946, *vice* Major K. N. Ghose.

Major F. W. Allinson is confirmed in the post of Surgeon Superintendent of the Presidency General Hospital, Calcutta, with effect from the 6th September, 1946.

Major F. M. Khan, M.B.B.S., is appointed as Port Health Officer, Calcutta, with effect from the 12th September, 1946.

Major C. B. D'Silva, M.B.B.S., is appointed Technical Officer, Central Institute, Kasauli, on probation for 1 year, with effect from the 2nd October, 1946.

Major C. Mani, M.B.B.S., is appointed Deputy Public Health Commissioner with the Government of India, is placed on deputation to the Government of Madras, with effect from the afternoon of the 17th October, 1946.

Major F. H. A. L. Davidson, M.B.B.S., on return from leave, is appointed to the post of Surgeon, Dacca, with effect from the 1st November, 1946.

Major W. J. Virgin, M.B.B.S., is appointed to the post of Surgeon, Dacca, with effect from the 1st November, 1946.

Major W. J. Virgin, M.B.B.S., is appointed to the post of Surgeon, Dacca, with effect from the 1st November, 1946.

Captain E. J. S. on return from leave is re-appointed as Surgeon of Ophthalmic Surgery, Medical College, Calcutta, with effect from the 1st November, 1946.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

as Captain

Mootlath Narayan Menon. Dated 15th March, 1945.

as Lieutenant

G. L. Awa. Dated 18th October, 1945.

LEAVE

Colonel A. K. Sahibzada, M.B.B.S., is granted leave preparatory to retirement for 28 months, with effect from the 15th October, 1946.

Lieutenant-Colonel W. H. Crichton, M.B.B.S., Director of Public Health, Calcutta, and Berar, proceeded on 4 months' leave with effect from the 1st November, 1946.

PROMOTION

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

as Lieutenant to be Captain

Captain Bawa. Dated 8th October, 1946.

RELINQUISHMENTS

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Lieutenant-Colonel. Their services are replaced at the disposal of the Government with effect from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Ty. Lieutenant Colonel M. A. Parthasarathy. Dated 28th March, 1946.

Ty. Lieutenant Colonel R. Viswanathan. Dated 6th June, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Lieutenant-Colonel:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Lieutenant-Colonel A. P. Venkateswami. Dated 30th April, 1946.

Ty. Lieutenant Colonel C. R. Krishnaswami. Dated 11th July, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service

subject to His Majesty's approval and are granted the honorary rank of Major:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major A. L. Sutherland. Dated 10th February, 1946.

Ty. Major P. K. Verma. Dated 8th March, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain R. S. T. Rajan. Dated 12th April, 1946.

Ty. Major J. K. Adrahvala. Dated 27th April, 1946.

Ty. Major S. P. Ramakrishnan. Dated 3rd May, 1946.

Ty. Major S. M. K. Wasti. Dated 17th May, 1946.

Major A. H. Khan. Dated 4th June, 1946.

Captain S. Purushotham. Dated 16th September, 1946.

Major N. L. Sharma. Dated 26th September, 1946.

Major D. D. Boovariwala. Dated 27th October, 1946.

The undermentioned officer is permitted to relinquish his commission on grounds of ill health and is granted the honorary rank of Major:—

JRPS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Ty. Major Profulla Koomar. Dated 27th July, 1946.

The undermentioned officer is permitted to relinquish his commission on release from Government of Madras and is granted the honorary rank of Major. His services are replaced at the disposal of the Government with effect from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

as Major. Dated 23rd April, 1946.

Major K. mentioned officers are permitted to relinquish their commissions on release from army service. The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major. Their services are replaced at the disposal of the Government with effect from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major H. K. Indra. Dated 4th March, 1946.

Major C. D. Torpy. Dated 30th April, 1946.

The undermentioned officer is permitted to relinquish his commission on release from army service and is granted the honorary rank of Major. His services are replaced at the disposal of the Punjab Government with effect from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Major A. A. Khan. Dated 14th May, 1946.

The undermentioned officers are permitted to relinquish their commissions on release from army service and are granted the honorary rank of Major. Their services are replaced at the disposal of the Government with effect from the date specified:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Major K. C. Dubey. Dated 1st April, 1946.

Ty. Major H. N. Dubey. Dated 24th June, 1946.

